Archives of Neurology and Psychiatry

VOLUME 33 FEBRUARY 1935 NUMBER 2

CRANIAL AND CERVICAL CHORDOMAS

A CLINICAL AND HISTOLOGIC STUDY

ALFRED W. ADSON, M.D.

JAMES W. KERNOHAN, M.D.

AND

HENRY W. WOLTMAN, M.D.

ROCHESTER, MINN.

In 1856 von Luschka [1] described small, mucus-containing excrescences which protruded from the basisphenoid and perforated the dura mater. The next year Virchow [2] saw similar nodules and designated them ecchordosis physaliphora. In 1858 Müller [3] suggested that these masses originated from remnants of the notochord which they resembled histologically, and also traced the notochord up to the sella turcica. Similar masses were frequently seen during the next thirty-five years, and in 1894 Ribbert and Steiner [4] found five examples of these small masses. In 1895 Ribbert [5] proved that they were of notochordal origin and that tumors originating from them should be called chordomas.

Most of the early examples of chordomas were found at necropsy and had not given rise to clinical symptoms. In 1910 the first chordoma arising from the region of the sacrum was described by Feldmann,[6] and since that time many others have been found arising from the caudal end of the notochord. The latest contribution to this group has been a study of ten additional cases by Fletcher,[7] and of the same cases by

---

Read before the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 4, 1934.

From the Sections on Neurologic Surgery (Dr. Adson), Pathologic Anatomy (Dr. Kernohan) and Neurology (Dr. Woltman) of the Mayo Clinic.

1. von Luschka, H.: Die Altersveränderungen der Zwischenwirbelknorpel, Virchows Arch. f. path. Anat. **9**:311, 1856.

2. Virchow, Rudolph, quoted by Stewart and Morin [15] and by Ribbert and Steiner.[4]

3. Müller, H., quoted by Stewart and Morin.[15]

4. Ribbert, Hugo, and Steiner, Hermann: Ueber die Ecchondrosis physalifora spheno-occipitalis, Centralbl. f. allg. Path. u. path. Anat. **5**:457 (June) 1894.

5. Ribbert, Hugo: Ueber die experimentelle Erzeugung einer Ecchondrosis physalifora, Verhandl. d. Kong. f. inn. Med. **13**:455, 1895.

6. Feldmann, I.: Chordoma Ossis Sacri, Beitr. z. path. Anat. u. z. allg. Path. **48**:630, 1910.

7. Fletcher, E. M.: Sacrococcygeal Chordomas, Thesis, University of Minnesota, December 1933.

Fletcher, Woltman and Adson,[8] with a complete review of the literature of sacrococcygeal chordomas up to date.

In spite of the fact that notochordal remnants are present in the nucleus pulposus of all intervertebral disks throughout life, very few chordomas have been found between the base of the skull and the sacrum. Most of the chordomas occurring in the vertebral column have been found in the cervical portion, and the literature was reviewed by Owen, Hershey and Gurdjian[9] in 1932; no further examples have been described since that time. There have been several excellent reviews of the literature on spheno-occipital chordomas in recent years; it would therefore serve no useful purpose to survey this literature again.

In the present contribution we report three new cases, in one of which the tumor arose from the clivus blumenbachii, in one from the spheno-occipital synchondrosis, and in one from the second cervical vertebra. These cases are interesting because knowledge has been limited concerning the response of these tumors to surgical intervention and roentgenotherapy, and because the tumor present in the cervical region in the third case had given symptoms for twenty years; at operation it was encapsulated and could be completely enucleated. In the histologic study of these tumors a new conception has been evolved, and further evidence has been secured in the controversy concerning the possible presence of glycogen in the cytoplasmic vacuoles of the cells.

REPORT OF CASES

CASE 1.—A woman, aged 29, came to the Mayo Clinic on June 15, 1927, because of diplopia and fatigue. In April 1922, eight weeks after delivery of an infant and for a period of four months, she had been troubled with diplopia, caused by turning inward of the left eye. There had been at the same time a mild left frontal headache. In October 1923, eight weeks after another confinement, she again had had diplopia and had observed that the left eye turned inward. There had also been some aching pain behind the eyes, which had lasted from six to twelve hours and had come once or twice each week. This time diplopia was permanent. Eleven months before she came to the clinic, the menses had stopped. She felt cold, became chronically tired, and said that it required the greatest effort "to get going." Her weight, which had been 115 pounds (52.1 Kg.) seven years before admission, had increased to 150 pounds (68 Kg.) within the last two years.

The patient was moderately obese and had a good color. She was lackadaisical and asked innumerable questions. Vision was 1/60 in the left eye and 6/60 in the right. There was right homonymous hemianopia with encroachment on the left temporal field (fig. 1). Both disks were pale. Movements of the left globe were moderately restricted in all directions; the left pupil was moderately dilated and immobile. The basal metabolic rate was — 18. Roentgen examination of the head gave negative results.

---

8. Fletcher, E. M.; Woltman, H. W., and Adson, A. W.: Sacrococcygeal Chordomas: A Clinical and Pathological Study, Arch. Neurol. & Psychiat., this issue, p. 283.

9. Owen, C. I.; Hershey, L. N., and Gurdjian, E. S.: Chordoma Dorsalis of Cervical Spine, Am. J. Cancer **16**:830 (July) 1932.

On July 26, 1927, a left frontoparietal craniotomy exposed a rounded mass covered with dura (fig. 2 *A*), 4 cm. in diameter, arising from the body of the sphenoid and extending into the middle fossa on the left. A crucial incision of the dura covering the mass permitted its contents to extrude (fig. 2 *B*), and a

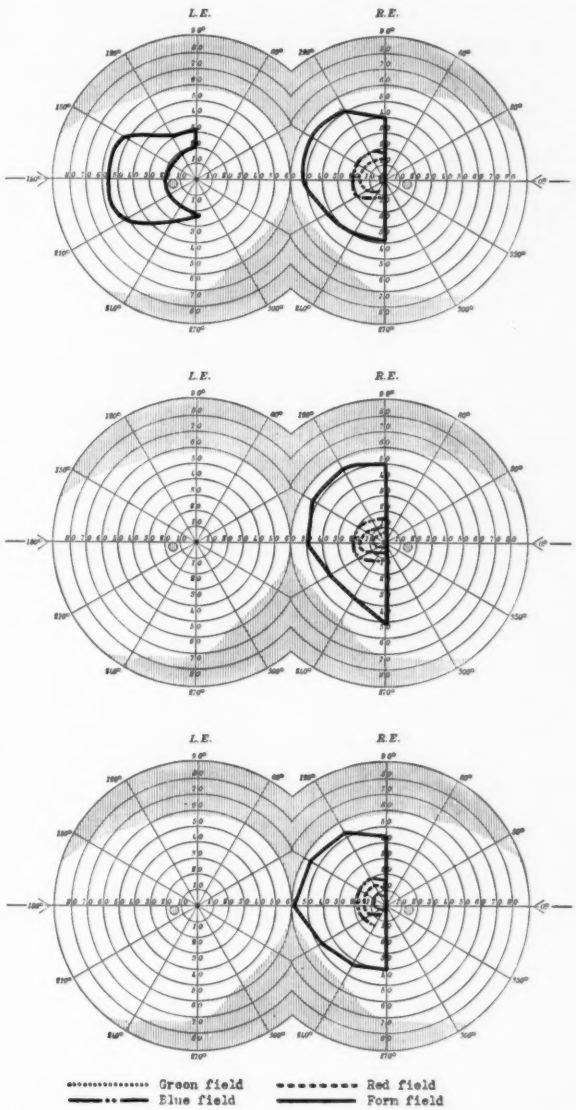


Fig. 1 (case 1).—Visual fields illustrating the character of visual loss.

brownish-gray, gelatinous, semisolid cellular substance was seen; there was no bleeding. Removal of the tumor was continued until all macroscopically identifiable tumor tissue has been taken away, leaving a pinkish, granular-appearing cavity which extended into the sphenoid. Roentgenotherapy followed.

Following operation an ulcer appeared on the left cornea, panophthalmitis developed and on August 24 the left globe was enucleated. Neurologic examination disclosed a slight impairment of superficial sensibility over the left half of the face. The patient's general condition was good. Menstruation was reestablished in October 1927.

On June 8, 1929, the patient returned. The menses had stopped again six months previously. The weight had increased to 191 pounds (86.6 Kg.). For three months she had become easily fatigued, especially in the left arm; there had been some dizziness, occasional nausea and slight uncertainty in gait.

The patient was obese and talkative and her conversation irrelevant. Vision was 6/7 in the right eye; the temporal field was lost, and the disk was pale. There was a slight left hemiplegia with the usual changes in tendon and plantar reflexes. The basal metabolic rate was —12. The concentration of hemoglobin was 59 per cent; the erythrocytes numbered 4,090,000 and the leukocytes, 13,000 per cubic millimeter of blood. Roentgenograms disclosed marked enlargement of the sella turcica.

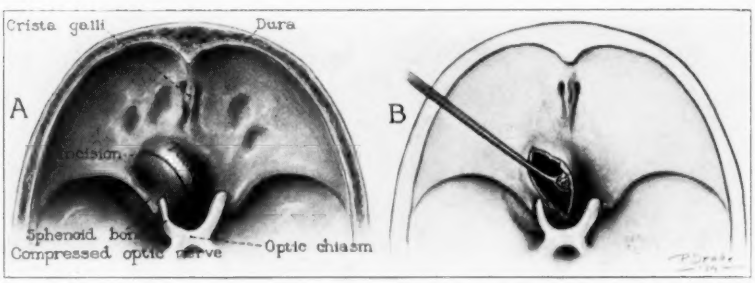


Fig. 2 (case 1).—Chordoma of the sphenoid bone with intracapsular enucleation.

Roentgenotherapy was administered without success. In a letter dated December 5 the patient reported that she was extremely weak; the left hemiplegia had progressed so that the left arm was almost helpless, and she had to be assisted in walking.

Microscopic Examination of Tissue.—The tissue had been placed in a 10 per cent solution of formaldehyde and after fixation was embedded in paraffin. Sections were cut and stained with hematoxylin and eosin, Van Gieson's stain, Meyer's mucicarmine and Best's stain for glycogen. The cellular arrangement of the neoplasm was that characteristic of chordomas and closely simulated notochordal tissue. The cells were growing in epithelial-like columns, separated from each other by a loose myxomatous stroma. There were many areas in which degeneration had occurred and in which there were no cells. The cytoplasm of the cells stained pink with eosin, and almost every cell contained numerous small vacuoles (fig. 3 *A*). Few large vacuoles were present, so that the individual cells were not wholly characteristic physaliphorous cells. The nuclei varied much in size and shape. They did not resemble epithelial nuclei, as they were not large and round, and only a few contained a centrally located, deeply staining, single nucleolus. The nuclei were for the most part hyperchromatic and seemed to be actively dividing, but mitotic figures were not present. Practically every nucleus contained several vacuoles (fig. 3 *B*) which varied in size so that they were typical

physaliphorous nuclei. The specific stain disclosed that some of the cytoplasmic vacuoles contained mucus; there was also a slight amount in the stroma, but most of the vacuoles did not react specifically and mucus was not demonstrable in the vacuoles of the nuclei. Since glycogen disappears rapidly after the death of tissue and is very soluble in water or in any fixative that contains water, fixation in formaldehyde precludes the use of specific stains for glycogen. This tumor had been fixed for more than six months in a solution of formaldehyde, so that in all probability the glycogen had entirely disappeared. Sections were prepared in the usual way, and after they had been embedded in paraffin they were stained with Best's carmine stain for glycogen after the method adopted by Meriwether [10] for

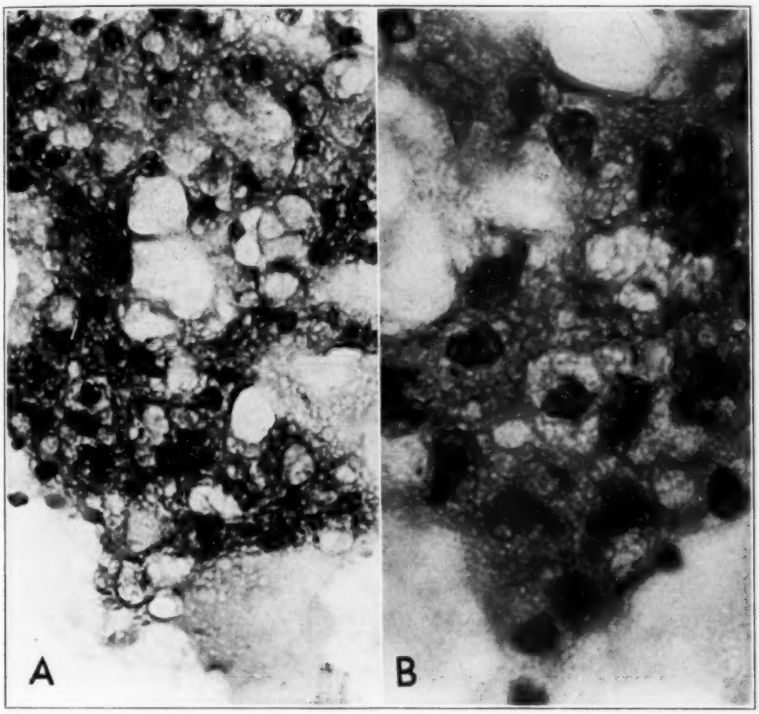


Fig. 3 (case 1).—*A*, the vacuoles in the physaliphorous cells are evident; × 400. *B*, in addition to the physaliphorous cells there are vacuolated or physaliphorous nuclei; × 1,050. Hematoxylin and eosin stain.

staining amebas in tissues. Many of the vacuoles in the tumor cells stained bright red and in others the nonvacuolated cytoplasm stained diffusely red. The myxomatous stroma between the cells remained unstained, as did the connective tissue and blood vessels in the tumor. The nuclear vacuoles also remained unstained. The color reaction after staining by this method has been considered specific for glycogen, but obviously the glycogen had been removed during fixation, so that the vacuoles contained some substance giving a nonspecific color reaction with Best's carmine stain.

10. Meriwether, L. S.: Identification of Amebas in Tissue, Proc. Staff Meet. Mayo Clin. **9**:95 (Feb. 14) 1934.

Previous workers who have obtained specific reactions with Best's carmine stain in chordomas may well have been observing this same nonspecific reaction which we found constantly in these three tumors, and which Meriwether [10] found in Endamoeba histolytica in tissues also fixed in formaldehyde.

Case 2.—A boy, aged 8 years, was brought to the Mayo Clinic on July 10, 1933, because of vomiting, indistinct speech and listlessness. On Jan. 12, 1933, he had fallen on the ice, striking heavily on the occiput. In March he had vomited occasionally, without nausea, especially on arising in the morning. At these times he had also complained of occipital headaches, which usually had lasted one or two hours but more recently had disappeared. Early in June it had been noted that speech was a little thick; toward the middle of June he had staggered slightly on walking; toward the end of June he had choked occasionally when swallowing, and on the day of his arrival fluid was regurgitated through the nose.

The boy was poorly nourished and somewhat lethargic. His speech had a nasal quality. His gait was slightly ataxic. Vision was 6/7 in both eyes; there was

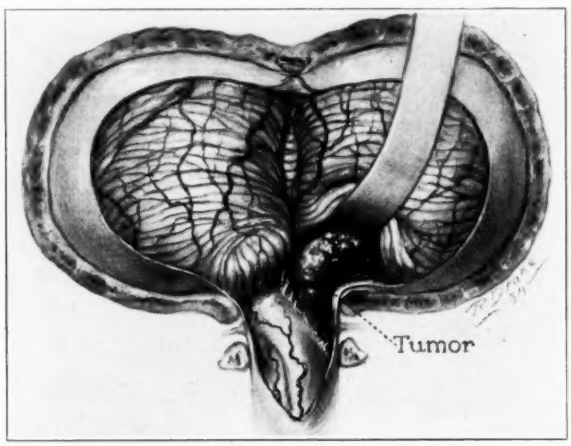


Fig. 4 (case 2).—Chordoma arising from the base of the occipital bone, compressing and displacing the medulla and pons to the left.

slight enlargement of the blind spots; the right disk was elevated by 5 diopters, and the left by 4 diopters. There were hemorrhages and exudates in the area of each disk. There was very slight horizontal nystagmus on looking toward the extreme right or left. On the right side the soft palate and tongue were almost completely paralyzed; the latter was moderately atrophied and fibrillating. Roentgenograms of the head disclosed slight separation of the coronal suture.

On July 14, 1933, bilateral suboccipital craniotomy revealed a conical mass arising extradurally, anteriorly and to the right of the pons and medulla. It extended into the foramen magnum (fig. 4), displacing medulla and spinal cord to the left against the opposite side of the foramen magnum (fig. 5). The dura mater was adherent to the mass, so that it was difficult to distinguish between the tumor and its covering. The tissue of the tumor was semisolid, pinkish and less dense than cartilage, but very vascular, which made a radical removal impossible. An extensive operation for decompression was performed, which included removal of the dorsal arch of the atlas.

Convalescence was rather stormy, since the patient had difficulty in absorbing the cerebrospinal fluid, and this necessitated numerous spinal punctures and repeated drainage of the posterior fossa. After three weeks he was dismissed from the hospital and received high voltage roentgen treatment. He was preparing to return home when pneumonia developed and he died.

Gross Examination of Tissue.—At necropsy bilateral bronchopneumonia was noted, but no other pathologic conditions of any significance in any of the organs of the thorax or abdomen. The operative wounds were healed. When the brain was removed cerebrospinal fluid was seen to be absent from the subarachnoid space; the convolutions were flattened and dry, and internal hydrocephalus, grade 2, involved all the ventricles. A tumor arose from the junction of the sphenoid and the base of the occipital bones; its point of attachment was 3 cm. in diameter, and the growth was mushroom-like in shape. The greatest diameter of the tumor

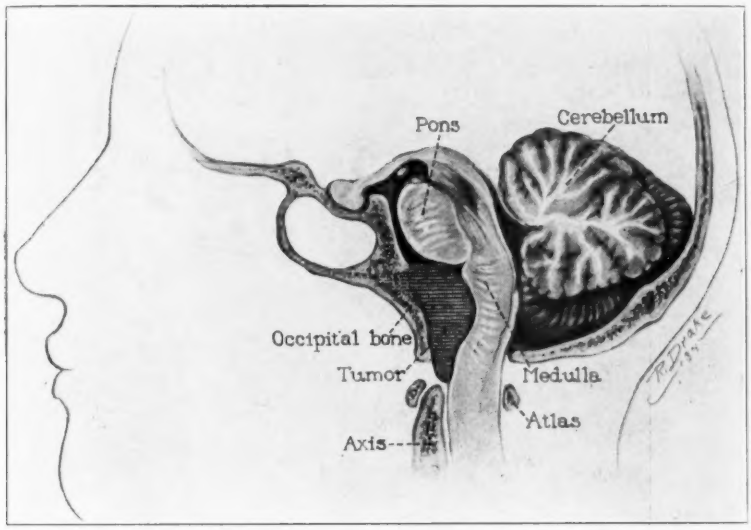


Fig. 5 (case 2).—Sagittal section showing the position of a chordoma of the occipital bone.

was 4 cm. and its height, 2.5 cm. This tumor was firm and nodular, had displaced the medulla oblongata forward and to the left and also had displaced and distorted the pons. It had formed a depression in the cerebellum to the right of the medulla oblongata, and had occluded Luschka's foramen on the right. The sella turcica and the bone down to the foramen magnum were removed with the tumor attached (fig. 6*A*). A roentgenogram was made of this bone, and it was found that in spite of the fact that the tumor originated from the spheno-occipital synchondrosis only slight erosion of the bone was visible (fig. 6*B*). The bone was then cut longitudinally through the sella turcica and pituitary body, and the tumor was seen to have invaded the bone extensively above and below the spheno-occipital synchondrosis (fig. 6*C*).

Microscopic Examination of Tissue.—Microscopic examination of the tissue removed at operation and at necropsy disclosed that the growth was a typical chordoma. The tumor cells were frequently arranged in rows or columns, some-

times as small clusters and occasionally as isolated cells. The cytoplasm varied in amount but usually contained several large, or numerous small, vacuoles; these were typical physaliphorous cells. The nuclei varied much in size and shape and only a few contained vacuoles. The stroma was vacuolated and stained bluish purple with hematoxylin and eosin. In some places fibrous tissue and fibroblasts were present in the stroma, and there were not many large vessels; these, however, were normal. With the mucicarmine stain the vacuoles in the cells for the most part stained specifically for mucus, but a few remained unstained. Toward the periphery of some of the cells the vacuoles were extremely small and numerous

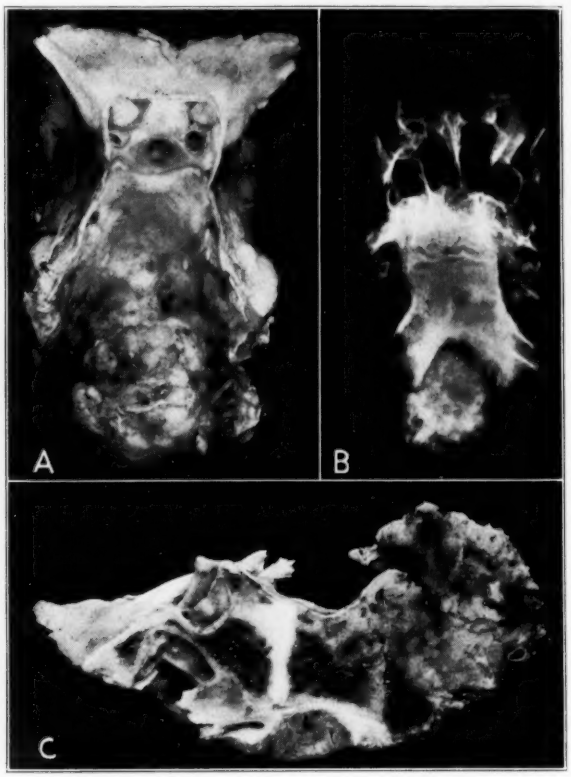


Fig. 6 (case 2).—*A*, photograph of the mushroom-like tumor projecting backward. It perforates the dura mater and is attached to the bone. *B*, roentgenogram of the spheno-occipital synchondrosis. Relatively little erosion of bone is evident. *C*, the sella turcica and clivus blumenbachii are cut in longitudinal section to the foramen magnum. The extensive invasion of the bone in the region of the spheno-occipital synchondrosis may be noted.

and merged gradually into the surrounding stroma, so that it was impossible at times to see clearly the boundaries of the cells. The vacuoles in the nuclei did not stain for mucus, but the stroma gave a strongly positive reaction. Special stains were of little help in the study of this tumor, as the content of the vacuoles which did not contain mucus or that of the vacuoles in the nuclei could not be identified.

The tissue of the tumor had been removed four and a half hours after death, and had been fixed in a 10 per cent solution of formaldehyde for several days. Any glycogen that had been present in the vacuoles of the tumor cells presumably had disappeared or had been dissolved. However, Best's carmine stain for glycogen produced a deep red reaction in many of the vacuoles, and the nonvacuolated cytoplasm stained a diffuse pink. Under high magnification the stained vacuoles and cytoplasm were granular and not homogeneous; the granules varied much in size. We again have considered this a nonspecific reaction, or else the content of the vacuoles and the granules in the cytoplasm is some form of glycogen not generally recognized. The vacuoles of the nuclei did not give the nonspecific reaction to Best's carmine stain for glycogen.

Comment on Cases 1 and 2.—In both cases the signs indicated the situation of the tumor, but its nature was not surmised. The observations in case 1 were similar to those of Bailey and Bagdasar's [11] first case, save that in their case the hemianopia was bitemporal. The situation of the tumor in case 2 of our series was similar to that in a case reported by Eckel and Jacobs,[12] and involvement of the twelfth cranial nerve was present in both; in our case the general symptomatology was that of tumor of the brain, whereas in theirs it was that of a tumor high in the cervical portion of the spinal cord.

Machulko-Horbatzewitsch and Rochlin [13] described, as typical of chordomas of the clivus, the onset with paralysis of the sixth cranial nerve and death due to bulbar involvement. Alajouanine, de Martel, Oberling and Guillaume [14] suggested that the combination of an osseous calotte and destruction of the posterior part of the sella turcica should make one think of a sphenobasilar chordoma. In neither case 1 nor case 2 did these suggestions find application. The inclusion of roentgenographic illustrations in the reports of cases when such changes occur may eventually lead to recognition of a characteristic picture that in some cases may aid in the preoperative diagnosis of chordomas.

CASE 3.—A woman of healthy appearance, aged 40, presented herself for examination on Nov. 12, 1924, complaining of pain in the left side of the neck and the left shoulder and arm and numbness of the left hand. The pain had been present for eleven years and had disturbed her sleep, especially when she lay on the left side. It was not aggravated by coughing. Removal of the tonsils three years before had not alleviated the discomfort. Recently there had been pain in the right shoulder and arm.

---

11. Bailey, Percival, and Bagdasar, Dumitri: Intracranial Chordoblastoma, Am. J. Path. **5**:439 (Sept.) 1929.

12. Eckel, J. L., and Jacobs, W. F.: Malignant Spheno-Occiptal Chordoma, J. Nerv. & Ment. Dis. **61**:471 (May) 1925.

13. Machulko-Horbatzewitsch, G. S., and Rochlin, L. L.: Klinik, Pathomorphologie und Histogenese der Chordome, Arch. f. Psychiat. **89**:222, 1930.

14. Alajouanine, T.; de Martel, T.; Oberling, C., and Guillaume, J.: Chordome de la région sellaire: Considérations anatomiques et cliniques, Rev. neurol. **1**:1221 (June) 1930.

The numbness had had its onset two years before she came to the clinic and involved the fingers of the left hand. It had been a constant handicap, causing her to drop and break dishes and making difficult the washing of clothes.

The principal findings were slight impairment in the speed of movements of the left forearm and hand, increased but equal tendon reflexes in all extremities, a positive Hoffmann test and extensor plantar responses which were more marked on the left. There were impairment of the sense of position of the left digits, marked astereognosis and moderate incoordination in performing the left finger-to-nose test; in the right upper extremity these discrepancies were very slight. The patient picked up pins and fastened the hooks of her dress only with the greatest difficulty. Vibratory sensibility was slightly impaired over the malleoli. Study with iodized poppy-seed oil 40 per cent failed to localize the lesion. The neck was freely movable, and roentgenograms of the cervical portion of the spine showed no abnormality. The patient declined an exploratory operation in view of the uncertain diagnosis.

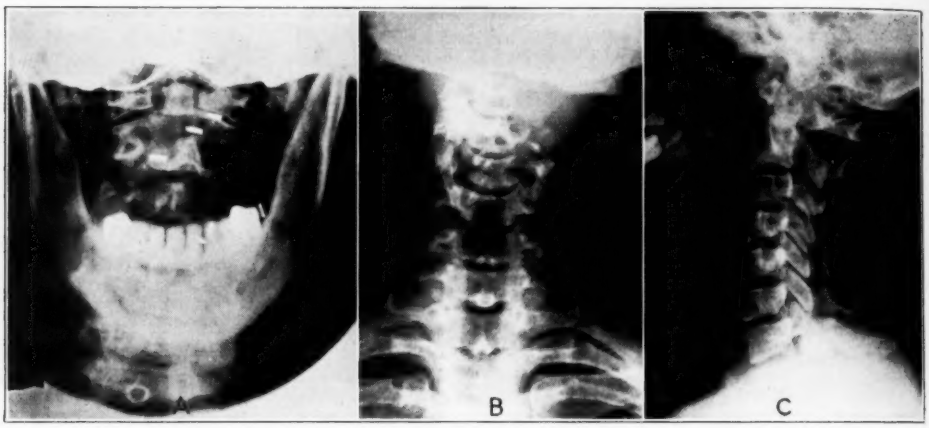


Fig. 7 (case 3).—*A*, lateral view showing erosion of the body and transverse process of the second cervical vertebra; *B*, anteroposterior view showing erosions of the first, second and third cervical vertebrae; *C*, anteroposterior view after operation showing the degree of erosion of the bone produced by the tumor.

On Aug. 12, 1931, the patient returned because of continued, although less intense, pain and because the left leg had occasionally given way, which worried her greatly.

She had much better use of the hands than in 1924; the neurologic signs noted then were still present, but were very slight, and there were added slight rigidity of the neck and marked impairment of vibratory sensibility over the malleoli and the iliac crests. Examination of the nasopharynx disclosed an even fulness of the left posterior pharyngeal wall opposite the tonsillar area. Roentgenograms revealed circumscribed destruction of the left halves of the first, second and third vertebrae (fig. 7). Exploratory operation was again declined. A supportive collar was advised.

On July 5, 1933, the patient again returned. There was still some pain; she was no more disabled than she had been but was greatly concerned over her uncertain future. She had not worn the collar.

The findings were the same as before, except that a vibratory fork placed over the malleoli was appreciated more readily. The clinical diagnosis was neurofibroma.

On July 7, 1933, the erosion on the left lateral surfaces of the cervical vertebrae and the bulging mass in the left nasopharynx caused one of us (Dr. Adson) to explore the mass through a cervical incision rather than through a wound for laminectomy (fig. 8). An incision along the posterior border of the sternocleidomastoid muscle exposed a nodular, lobulated, encapsulated mass which measured

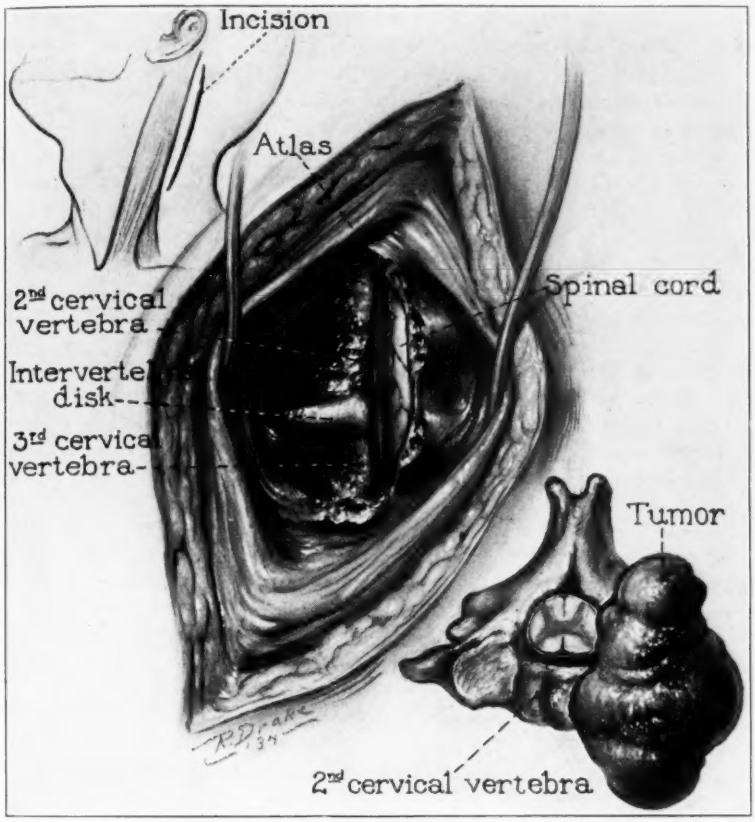


Fig. 8 (case 3).—Drawing showing the erosion of bone and compression of the cord by the encapsulated cervical chordoma.

7 by 6 by 4 cm. The tumor arose in the vicinity of the second cervical vertebra, and since the surgeon had not previously encountered a chordoma in this region, the growth was thought to be a neurofibroma. The tumor was definitely encapsulated and contained nodules that extended in all directions, one of which grew posterior to the pharyngeal wall and accounted for the fulness in the left side of the nasopharynx. Other nodules had caused erosion of the borders and transverse processes of the second and third cervical vertebrae and parts of the laminae of the atlas, axis and third cervical vertebra. The body of the axis was eroded at

least one third of the way through. The intervertebral disks were all preserved. Subsequent laminectomy was unnecessary, for it was possible to remove all intraspinal nodules through the eroded laminae. The dura was not opened; in several areas, however, it was so thin that the arachnoid bulged through like blisters. The masses were all encapsulated and were lifted out of the bony pits without breaking. The tumor itself contained yellow, necrotic portions, although the greater portion was friable, semisolid and pearl gray.

Convalescence was uninterrupted and of the neurologic signs only bilateral extensor plantar responses remained. The patient was dismissed on July 27.

Macroscopic and Microscopic Examination of Tissue.—The tumor was firm, rounded, nodular and encapsulated. It had a colloid appearance, but there were some yellowish portions which simulated the degenerated portions so constantly seen in neuromas arising from the eighth cranial nerve.

The tissue which had been removed at operation had been placed in a 10 per cent solution of formaldehyde for fixation. With the hematoxylin and eosin stain the arrangement of the cells did not seem to be that of a typical chordoma, since they only occasionally formed columns or assumed an epithelial appearance. The cells were lying singly or in small groups and had a basic-staining, homogeneous matrix. The cells were characteristic of notochordal cells, for most of them had vacuoles in their cytoplasm (physaliphorous cells). The vacuoles were usually small and numerous, but occasionally one large vacuole was seen, almost completely replacing the cytoplasm and displacing the nucleus to one side of the cell body. The outline of the cells was usually clear and distinct, but occasionally it merged gradually into the surrounding stroma in which vacuoles were not present. The nuclei varied in size and appearance; they were usually oval in shape, but some bizarre forms were to be seen. They were pale-staining, and many had one large, deeply staining, centrally situated nucleolus. With special nuclear stains most of the cells were seen to contain one or more nuclear vacuoles—typical physaliphorous nuclei, such as were first described by Stewart and Morin.[15] Mitotic figures were not found in this tumor. In the stroma, especially near blood vessels, there were numerous small collections of lymphocytes, plasma cells and eosinophilic leukocytes. The blood vessels were normal. With the Van Gieson stain there was little adult connective tissue in the stroma. Meyer's mucicarmine stain showed that there was much mucus in the stroma of the tumor and that many of the cytoplasmic vacuoles of the cells contained mucin. However, many vacuoles did not contain any demonstrable mucin, and the vacuoles of the nuclei did not respond specifically for mucus. With the stain for glycogen, as in the other tumors, many vacuoles in the cytoplasm stained bright red, while some remained unstained, as did the nuclear vacuoles. The stroma, the connective tissue and the blood vessels did not stain with Best's carmine stain.

COMMENT

Vertebral chordomas, except in the sacrococcygeal region, are decidedly infrequent. The next most common situation is the cervical region. Owen, Hershey and Gurdjian, in 1932, added a ninth case to the cervical group they had succeeded in collecting from the literature.

---

15. Stewart, M. J., and Morin, J. E.: Chordoma: A Review with Report of a New Sacrococcygeal Case, J. Path. & Bact. **29**:41, 1926.

In 1933 Joyce [16] reported the case of a man, aged 46, whose symptoms began immediately following injury and were those generally suggestive of involvement of the pyramidal decussation; the tumor sprang from the second cervical vertebra, and may perhaps be added to those listed as of odontoid origin. Recurrence was followed by a second operation. In Simon's [17] case, that of a woman, aged 57, the symptoms included dysphagia and pain and weakness of the right shoulder. The tumor was situated opposite the fourth, fifth and sixth cervical vertebrae, and had eroded the body of the third. Operation was followed by recurrence in the wound and presumably extension into the plexus.

In the second case reported by Hutton and Young,[18] that of a man, aged 49, there were compression of the thoracic portion of the cord and erosion of the fourth, fifth and sixth thoracic vertebrae. Although in the case of a woman, aged 36, described by Jelliffe and Larkin,[19] the tumor originated in the cranium and was attended by extensive palsy of the cranial nerves and marked confusion and delirium, metastatic growths found their way to the midthoracic region, where a mass was palpable, and resulted in the production of a transverse level of sensory loss, weakness of the lower extremities and extensor plantar reflexes. The patellar and achilles tendon reflexes were absent.

The lumbar region too is not exempt. This is shown by the case reported by Davison and Weil,[20] that of a man, aged 64, whose third and fourth lumbar vertebrae were involved. Moreover, in the case reported by Zollinger,[21] that of a woman, aged 62, a chordoma lay opposite the entire lumbar portion of the spine and had produced paralysis of motion and loss of sensation. A unique case was reported by Morpurgo [22] in which a chordoma was found in the lumbar region of an osteomalacic mouse.

So far a preoperative diagnosis of chordomas has been made only through biopsy, a procedure that is restricted to tumors of the sacro-

---

16. Joyce, T. M.: Chordoma of Second and Third Cervical Vertebrae, S. Clin. North America **13**:85 (Feb.) 1933.

17. Simon, Otto: Das vertebrale Chordom, Deutsche Ztschr. f. Chir. **241**: 805, 1933.

18. Hutton, A. J., and Young, Archibald: Chordoma: A Report of Two Cases: A Malignant Sacrococcygeal Chordoma and Chordoma of the Dorsal Spine, Surg., Gynec. & Obst. **48**:333 (March) 1929.

19. Jelliffe, S. E., and Larkin, J. H.: Ueber ein malignes Chordom mit Symptomen von Seiten des Gehirns und Rückenmarks, Ztschr. f. d. ges. Neurol. u. Psychiat. **5**:590 (April) 1911.

20. Davison, Charles, and Weil, Arthur: Malignant Chordoma of the Lumbar Region, Arch. Neurol. & Psychiat. **19**:415 (March) 1928.

21. Zollinger, Robert: Chordoma of the Third Lumbar Vertebra: Report of a Case, Am. J. Surg. **19**:137 (Jan.) 1933.

22. Morpurgo, B., quoted by Coenen, Hermann: Das Chordom, Beitr. z. klin. Chir. **133**:1, 1925.

coccygeal group and to those that make their way into the nasopharynx, either from the skull, as in the cases reported by Cantor and Stern [23] and by Selinsky,[24] or from the cervical portion of the spine. But biopsy, too, may present difficulties, as was experienced by Hirsch,[25] from whose patient repeated specimens taken from a tumor in the tonsillar region resulted in such a wide variety of diagnoses and comments by eminent pathologists as almost to drive him to despair; a terse diagnosis of chordoma finally settled the issue. Until the pathologist had been informed that the tumor extended into the retropharyngeal space, he had had, as may well be imagined, great mental hazards to surmount.

It has been suggested that a diagnosis of chordoma arising from the clivus blumenbachii or spheno-occipital synchondrosis could be made only with the aid of roentgenography. In case 2 of our series, in spite of the fact that the tumor had originated from the region of the spheno-occipital synchrondrosis and had invaded the surrounding bone, little evidence of destruction of bone was seen in the postmortem roentgenogram. Obviously, then, visualization of the tumor in situ would be very difficult or almost impossible. In case 1 there was no demonstrable destruction of bone, and only the secondary signs or those from neighboring involvement led to a diagnosis. Operative intervention relieved many of the signs of dyspituitarism, at least temporarily, and even the menses returned to normal. Roentgen therapy is of doubtful value, although this group of tumors is too small to allow conclusions to be drawn from it. Most chordomas have a tendency to invade the surrounding bone and soft tissues, so that complete removal is impossible, and thus local recurrence and extension are almost certain. Case 3 is unique in this respect, as the tumor was definitely and completely encapsulated and was thus enucleable. It had eroded, but not invaded, the adjacent bone, and behaved grossly more like a neurofibroma than like a chordoma.

The histologic features of all three tumors were characteristic of chordomas and closely simulated embryonic notochord. Some of the vacuoles of the physaliphorous cells contained mucus, and the content of the others was not demonstrable. It has been claimed that these vacuoles contain glycogen, but it is often impossible to obtain fresh tissue and to fix it immediately in absolute alcohol, which is necessary for the microchemical identification of this substance; therefore it is difficult to prove or to disprove this claim. The tissue from all of our three tumors had been fixed in formaldehyde, which is an aqueous solu-

---

23. Cantor, M., and Stern, L. D.: Spheno-Occipital Chordoma: Report of a Case, Arch. Neurol. & Psychiat. **30**:612 (Sept.) 1933.

24. Selinsky, Herman: Intracranial Chordoma: Report of a Case, Arch. Neurol. & Psychiat. **28**:413 (Aug.) 1932.

25. Hirsch, Caesar: Zur Frage des malignen Chordoms, Ztschr. f. Hals-, Nasen- u. Ohrenh. **28**:140, 1931.

tion and in which glycogen is extremely soluble; yet Best's carmine stain used on sections of this tissue which had been embedded and cut in paraffin gave a strongly positive result. Control sections from other tissues, as the liver, and from such tumors as chondromas did not give positive reactions. It is doubtful if the content of the cellular vacuoles is glycogen, but it is possibly paraglycogen or some allied substance. Further investigation of the content of these vacuoles is necessary to determine its true nature. The nuclear vacuoles did not give a positive reaction with the stain for glycogen. It is at least possible that previous workers who have demonstrated glycogen in chordomas were obtaining a nonspecific reaction such as we observed. They did not mention having tried the stain for glycogen after the tumor tissue had been fixed in formaldehyde or in some fixative containing water.

THE NUCLEI OF THE POSTERIOR FUNICULI IN MACACUS RHESUS

AN ANATOMIC AND EXPERIMENTAL INVESTIGATION

A. FERRARO, M.D.

AND

S. E. BARRERA, M.D.

NEW YORK

Because of the uncertainty still reigning as to the number of cell groups to be found in the nuclei of the posterior funiculi, we thought it advisable to undertake a study of the normal cellular arrangement of these nuclei in Macacus rhesus, and then to establish experimentally their anatomic connections.

We have particularly been concerned with the morphology and connections of the so-called external or lateral cuneate nucleus which has received different names from various investigators, namely, external portion of the restiform nucleus (Clarke [1]), Monakow's nucleus (Winkler,[2] Kappers [3] and others), nucleus carporis restiformis (Gudden, Wernicke and Ziehen), Blumenau's nucleus (Geist [4] and Zeehandelaar [5]), accessory cuneate nucleus (Ranson [6]) and pars magnocellularis funiculi posterioris (Gagel and Bodechtel [7]).

Study of serial sections of the normal brain of a monkey (Macacus rhesus) has resulted in our distinguishing in the nuclei of the posterior

---

From the Department of Neuropathology, New York State Psychiatric Institute and Hospital.

1. Clarke, J. L.: Researches on the Intimate Structure of the Brain, Phil. Tr. London **158**:269, 1868.

2. Winkler, C.: Manuel de neurologie, Haarlem, Netherlands, Erven F. Bohn, 1927, pt. 3.

3. Ariëns Kappers, C. U.: Vergleichende Anatomie des Nervensystems der Wirbeltiere und des Menschen, Haarlem, Netherlands, Erven F. Bohn, 1920.

4. Geist, F. D.: The Brain of the Macacus Rhesus Monkey, J. Comp. Neurol. **50**:333, 1930.

5. Zeehandelaar, I.: Ontogenese und Phylogenese der Interstrangkerne in Verband mit der Sensibilität, Folia neurol. **12**:1, 1921.

6. Ranson, S. W.; Davenport, H. K., and Doles, E. A.: Intramedullary Course of the Dorsal Root Fibers of the First Three Cervical Nerves, J. Comp. Neurol. **54**:1 (Feb.) 1932.

7. Gagel, O., and Bodechtel, G.: Die Topik und feinere Histologie der Ganglienzellgruppen in der Medulla oblongata und im Ponsgebiet mit einem kurzen Hinweis auf die Gliaverhältnisse und die Histopathologie, Ztschr. f. Anat. u. Entwcklngsgesch. **91**:130, 1929.

funiculi three large groups of cells, namely, the nucleus gracilis (Goll), the nucleus cuneatus (Burdach) and the external cuneate nucleus.

A detailed description of the various cellular groups in a normal monkey follows.

At the level of the crossing of the pyramis it may be seen that in the posterior funiculi a few cells begin to appear in the fasciculus gracilis. The fibers of the posterior funiculi are still numerous and the substantia gelatinosa of Rolando is quite evident in the semilunar aspect.

At a slightly higher level the cells of the nucleus gracilis have increased considerably in number and occupy a longitudinal stretch from the ventral to the dorsal aspect of the column. There is a beginning lamination of the cell group in the anteroposterior direction. The most caudal portion of the nucleus cuneatus makes its appearance.

At a still higher level the nucleus cuneatus is better developed and is seen ventral to the nucleus gracilis. Its cells are slightly larger than the cells of the nucleus gracilis, the lamination of which is evident. The cells of the nucleus gracilis are fundamentally of two types. One type is represented by medium-sized cells, generally slightly elongated and at times showing a slightly vesicular cytoplasm and eccentric nucleus. The other type is represented by small cells with finely granular cytoplasm and a rounded nucleus. A much more laterally located nucleus now makes its appearance. It is a large cell nucleus located at the most external portion of the medulla, dorsal to the substantia gelatinosa of Rolando. Its cells are vesicular and larger than the cells of both the nucleus gracilis and the nucleus cuneatus. The nucleus of the cells is eccentric and the morphology of the cellular elements recalls that of the cells of Clarke's column. This nucleus corresponds to the external cuneate nucleus.

At a still higher level (fig. 1) the nucleus gracilis has acquired a triangular aspect and can be seen in the fullest extent of its development in the most medial and dorsal portion of the posterior funiculus. A winglike development forms the lateral portion of this nucleus, in which lamination is evident. The nucleus cuneatus is acquiring a roundish aspect ventral and lateral to the nucleus gracilis. The external cuneate nucleus has acquired a definitely oval shape, and bridges of nerve cells are seen crossing the white substance toward the nucleus cuneatus.

As one proceeds cephalad the nucleus gracilis diminishes in size, though still occupying the most dorsal and medial area of the posterior funiculus. The nucleus cuneatus has acquired a larger development and its full round portion is distinctly visible. The number of nerve cells now forming the nucleus is considerable and the nucleus as a whole is practically as large in volume as the nucleus gracilis. Its cells are medium-sized and a tendency to lamination in concentric circles is now noticeable. Lateral to the cuneate nucleus, in the area separating its round portion from the external cuneate nucleus, new cells are seen, some of which are the continuation of the bridges of cells which have been described in the lower levels. The latter nucleus is fully developed and its cells are distinctly larger than the cells of either one of the other nuclei. Its shape is oval and the structure occupies an oblique position, underlying the oblique course of the dorsospinocerebellar tract.

At a higher level the nucleus cuneatus is seen distinctly formed by two portions, a round portion which might be called the pars rotunda, and a triangular portion which occupies the space between the external cuneate nucleus and the pars rotunda (fig. 2). This triangular portion, which might be termed the pars triangularis,

has the shape of an isosceles triangle with a dorsal apex and a ventrally directed base. The division into pars rotunda and pars triangularis seems to be due to the initial course of some of the arcuate fibers, which at this level have a definite dorsoventral direction at their origin. The distribution and the size of the cells in this area are, however, typical enough to justify its anatomic distinction as the pars triangularis. The nerve cells constituting this portion, though in the majority of the small type, are intermingled with some of the large cellular elements bridging to the external cuneate nucleus.

The whole nucleus cuneatus occupies now a more lateral position than at its caudal extremity. The whole structure follows, therefore, an oblique course from the lower to the upper planes and from a middle to a lateral location. At the

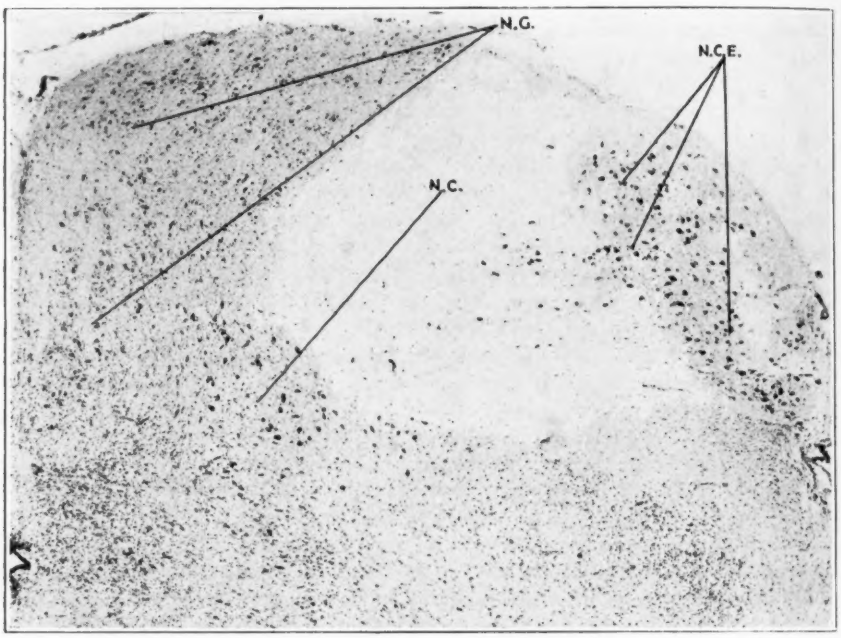


Fig. 1.—From a section of the medulla oblongata of a normal monkey. The figure illustrates the triangular aspect of the nucleus gracilis and its apparent lamination. The nucleus cuneatus is ventrally located. Along the lateral surface of the medulla, the external cuneate nucleus is visible. Nerve cells are seen bridging between the external cuneate nucleus and the nucleus proper. *N.G.* represents the nucleus gracilis; *N.C.*, the nucleus cuneatus, and *N.C.E.*, the external cuneate nucleus. Nissl stain.

base of the pars rotunda some large cells are also seen which are in size and shape like the large cells of the external cuneate nucleus.

With the development of the nuclei of the twelfth and tenth cranial nerves, the nucleus gracilis is seen to shift its position to occupy the most dorsal portion of the fasciculus gracilis, a deviation, in other words, of its upper portion toward the lateral aspect of the medulla.

At the level of the caudal end of the dorsal nucleus of the vagus just before the central canal opens into the fourth ventricle, the pars triangularis of the

nucleus cuneatus discloses more numerous large cells, a condition which contributes to a closer relationship between the pars rotunda of the cuneate nucleus and the large cells of the external cuneate nucleus. The nucleus gracilis becomes smaller and smaller and is decidedly confined to the more dorsal aspect of the medulla.

At the extreme caudal portion of the eminentia vestibularis it may be seen that the nucleus gracilis has practically disappeared and that only the upper portion of the nucleus cuneatus is still visible, in close contact with the upper portion of the external cuneate nucleus. The nucleus cuneatus contains numerous large cells, particularly along its periphery.

At the level at which the nuclei of the twelfth and tenth nerves are fully developed a certain number of cells are still seen forming the cephalic portion of

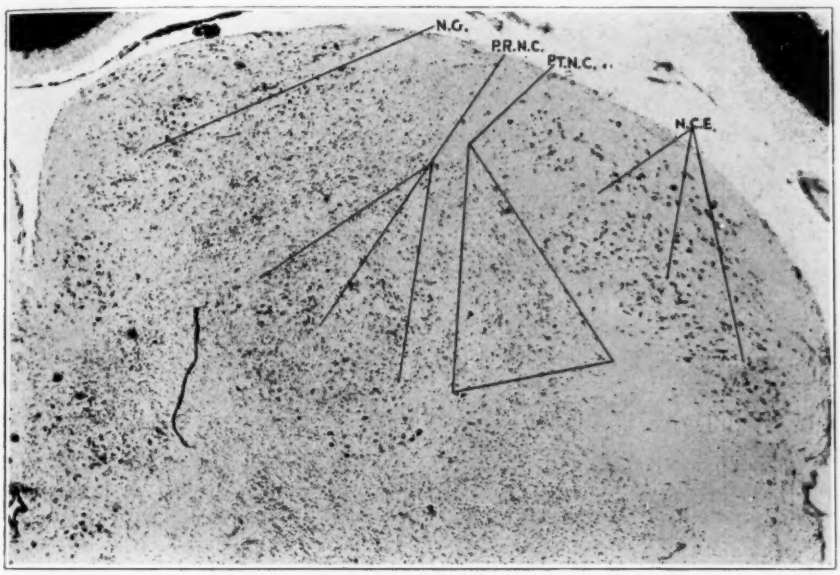


Fig. 2.—From a section of the medulla oblongata of a normal monkey. The figure illustrates the two divisions of the cuneate nucleus, the pars rotunda and the pars triangularis. The nucleus gracilis has become smaller and is located in the most dorsal medial portion of the section. The external cuneate nucleus is fully developed and large cells are seen bridging between the external cuneate nucleus and the cuneate nucleus proper. In addition a few large elements of the same type are seen at the base of the pars rotunda. *N.G.* represents the nucleus gracilis; *P.R.N.C.*, the pars rotunda of the nucleus cuneatus; *P.T.N.C.*, the pars triangularis of the nucleus cuneatus, and *N.C.E.*, the external cuneate nucleus. Nissl stain.

the nucleus cuneatus, and slightly lateral and ventral to it are to be seen the cells of the external cuneate nucleus, surrounded by the bulk of the fibers of the corpus restiforme.

As the sections proceed cephalad, the eminentia vestibularis is surrounded ventrally by larger cellular elements which have no direct contact with the remaining cells of the nucleus cuneatus. The cells of this nucleus are few and

occupy the area immediately medial to the remaining cells of the external cuneate nucleus located in the inner margin of the corpus restiforme.

At the zone of entrance of the dorsal roots of the eighth nerve into the vestibular area a very few cells of the external cuneate nucleus are still seen reaching the ventral portion of the vestibular nuclei. No further trace of the nucleus cuneatus is found. Finally, at a slightly higher level, where the ventral portion of Deiters' nucleus makes its appearance, no more trace is found of the external cuneate nucleus.

EXPERIMENTAL WORK

In order to establish experimentally the connections of the various groups of cells of the posterior funiculi four types of experiments were devised on monkeys (Macacus rhesus), two of which were repetitions of those of von Monakow. The latter consisted of: (*a*) section of the inferior cerebellar peduncle and (*b*) hemisection of the spinal cord. The two additional experiments consisted of: (*c*) complete removal of the cerebellum and (*d*) dorsoventral section of the lemniscus medialis in the region of the medulla oblongata.

The purpose of these experiments was to establish the topography of the cell groups which would suffer most severely from the operative procedures and from this to deduce the course of the axons arising from these cell groups. We intended also to find out if, in harmony with various statements in the literature, there are to be considered in the posterior funiculi, in addition to the nucleus cuneatus and nucleus gracilis, two other distinct groups of cells: the external cuneate nucleus and the nucleus of the corpus restiforme (Winkler).

Complete Removal of the Cerebellum.—Following complete removal of the cerebellum we noticed no changes of importance taking place in the nucleus gracilis and nucleus cuneatus. On the other hand, a considerable reduction of cells, amounting to total disappearance, was to be seen in the most caudal segment of the external cuneate nucleus. This thus definitely establishes the fact of the different connections of this nucleus and of the nucleus gracilis and nucleus cuneatus.

Figure 3 illustrates a cross-section of the middle level of the medulla oblongata in a monkey, the cerebellum of which had been totally removed three months previously. At this level both the nucelus gracilis and the nucleus cuneatus can be recognized, the cells of the nucleus cuneatus being somewhat larger than those of the nucleus gracilis. Contrasting with the richness in cells of the two aforementioned nuclei is the considerable disappearance of cells in the external cuneate nucleus.

It may be seen also that a normal number of cells is present in the nucleus gracilis and in both the pars rotunda and the pars triangularis of the nucleus cuneatus. In the external cuneate nucleus a few large cells are still present, though they are few.

More cephalad a normal content of cells is present in the nucleus cuneatus (pars rotunda and pars triangularis) and in the remaining portion of the nucleus gracilis. It may be seen also that some of the large cellular elements normally found at the base of the pars triangularis of the nucleus cuneatus are still present, though reduced in volume (fig. 4).

Higher up a few nerve cells still remain in the external cuneate nucleus, whereas the number of cells in the nucleus cuneatus and the remaining portion of the nucleus gracilis occupying the most dorsal aspect of the posterior funiculus appears normal. At this level a few of the bridge cells connecting the external cuneate nucleus with the cuneate nucleus are also present, though the individual nerve cells appear somewhat smaller.

At higher levels a very few cells are still present in the external cuneate nucleus, up to the plane where this nucleus reaches the ventral portion of the eminentia vestibularis. No further appreciable changes are noticed in the remaining portion of the nucleus cuneatus.

Section of the Inferior Cerebellar Peduncle.—Following complete section of the inferior cerebellar peduncle at the level of entrance of the roots of the eighth

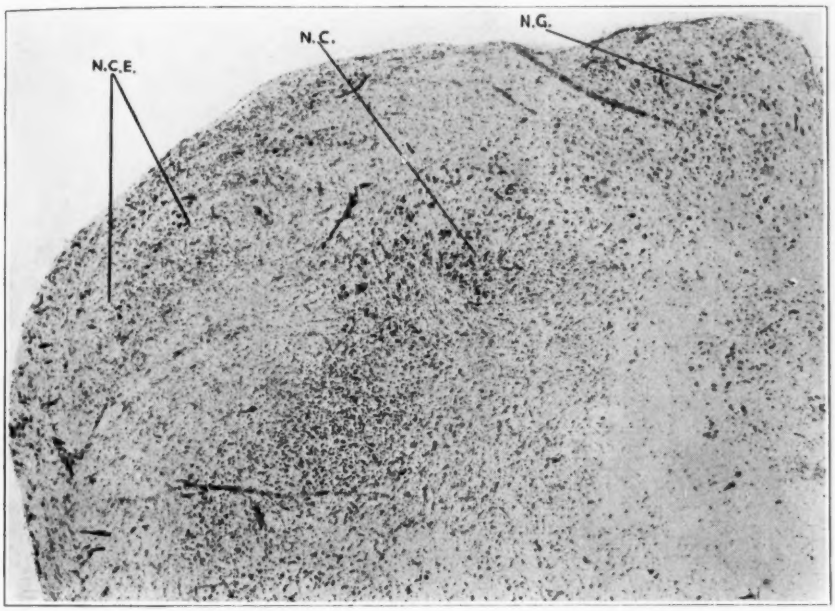


Fig. 3.—From a section of the medulla oblongata of a monkey, five months after the removal of the cerebellum. The figure illustrates the almost complete disappearance of the nerve cells in the external cuneate nucleus, contrasting with the normal amount of nerve cells in the nucleus gracilis and nucleus cuneatus. *N.C.E.* represents the external cuneate nucleus; *N.G.*, the nucleus gracilis, and *N.C.*, the nucleus cuneatus. Nissl stain.

nerve, the cells of the external cuneate nucleus disappeared and only a few of them were found distributed here and there at various levels. Contrasting with such a disappearance of cells in the external cuneate nucleus was the intactness of the nucleus gracilis and nucleus cuneatus. The picture thus resulting was like that following removal of the whole cerebellum.

The conclusion is therefore justified that following section of the inferior cerebellar peduncle practically all the fibers originating from the nerve cells of the external cuneate nucleus are severed, thus confirming their connection with

the cerebellum via the inferior cerebellar peduncle. The connections of the nucleus gracilis and nucleus cuneatus follow, of course, another pathway via the medial lemniscus.

Hemisection of the Cord at the Level of the Second to the Third Cervical Segments.—Repeating von Monakow's experiment of hemisection of the spinal cord in the rabbit, one monkey was used in which a lesion was made, destroying in the spinal cord all of the lateral funiculus and the fasciculus cuneatus. The fasciculus gracilis was preserved, as in von Monakow's original experiment. In the gray matter it was found that most of the cells of the anterior horn had disappeared, though the lesions did not involve the gray horns directly.

As a result of the lesion the nucleus gracilis and nucleus cuneatus as well as the external cuneate nucleus do not disclose any appreciable diminution in number of nerve cells.

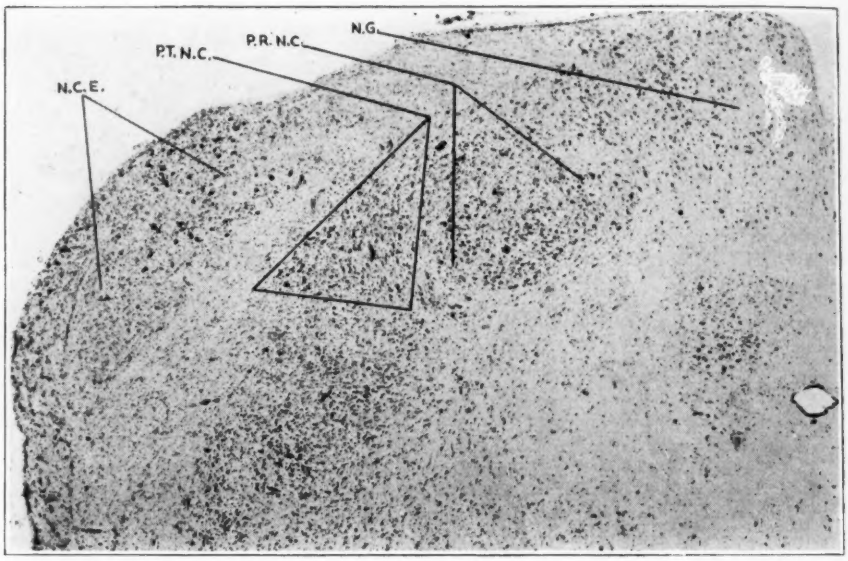


Fig. 4.—From a section of the medulla oblongata of a monkey, five months after the removal of the cerebellum. The picture illustrates the persistence of a few large cells in the oral end of the external cuneate nucleus, contrasting with the normal amount of nerve cells in the remaining portion of the nucleus gracilis and in both the pars triangularis and pars rotunda of the nucleus cuneatus. *N.C.E.* represents the external cuneate nucleus; *N.G.*, the nucleus gracilis; *P.T.N.C.*, the pars triangularis of the nucleus cuneatus, and *P.R.N.C.*, the pars rotunda nucleus cuneatus. Nissl stain.

At a low level of the medulla it may be seen that the pars rotunda and pars triangularis of the nucleus cuneatus contain a normal number of nerve cells and that the bridge cells between the external cuneate nucleus and the cuneate nucleus proper are distinctly recognizable. The nucleus gracilis is seen occupying the dorsal portion of the posterior funiculus. What appears to be of importance among the cells of the various nuclei, particularly of the cuneate and external nuclei, is the presence of a marked glial reaction which is to be related to degenerated fibers resulting from section of the fasciculus cuneatus at a lower level.

At a higher level, there are still a normal number of large cells in the external cuneate nucleus, entirely surrounded at this level by the fibers of the corpus restiforme. The pars rotunda and pars triangularis of the cuneate nucleus show no appreciable variations from the normal, except for the presence of increased glial nuclei.

At a still higher level, the cells of the cuneate and external cuneate nuclei are normal in number, not differing in this respect from the cells to be seen at the same level of the normal animal. The main point of difference between the nerve cells in this case and the cells of the normal nuclei is that in the experimental case the cells of the aforementioned nuclei are somewhat smaller than the normal. The smallness of the cells is to be correlated with the fact that proprioceptive impulses no longer reach these structures because of the interruption of fibers in the fasciculus cuneatus at the level of the hemisection.

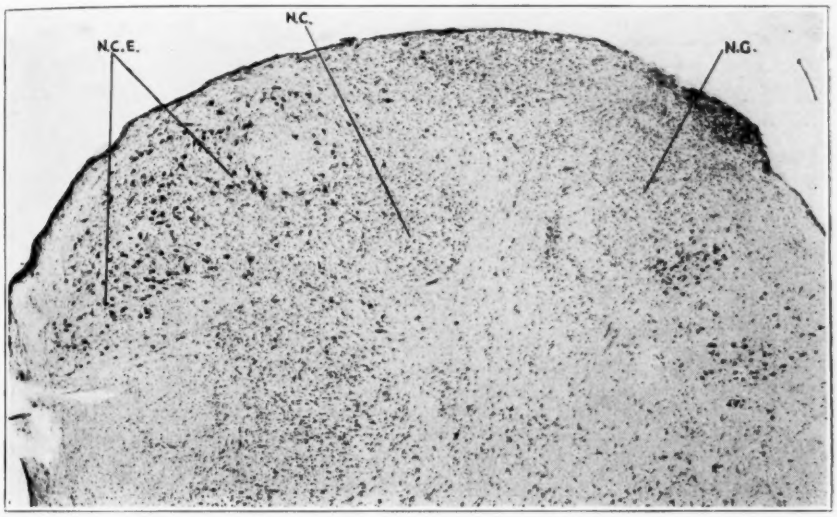


Fig. 5.—From the medulla oblongata of a monkey twenty-five days after the dorsoventral splitting of the decussation of the medial lemniscus. The picture illustrates the disappearance of nerve cells in the nuclei gracilis and cuneatus contralateral to the vertical section of the lemniscus. Note the contrast of the normal content in nerve cells of the external cuneate nucleus with the complete disappearance of the nerve cells in the nuclei gracilis and cuneatus. *N.C.E.* represents the external cuneate nucleus; *N.G.*, the nucleus gracilis, and *N.C.*, the nucleus cuneatus. Nissl stain.

Lesion of the Medial Lemniscus in the Medulla Oblongata.—A unilateral lesion of the lemniscus was made with a fine knife in a dorsoventral and frontocaudal direction. The lesion entered the medulla from the floor of the fourth ventricle, reaching the base of the pyramis. Serial sections of the lesion disclose that a great majority of the fibers of the lemniscus have been destroyed; part of them were involved in the lesion at the level of their crossing, but most of them after the crossing has occurred.

As a result of the destruction of the medial lemniscus most of the cells of the nucleus gracilis and nucleus cuneatus disappeared on the side contralateral to the

lesion. A comparison of figure 5 with figure 6 will clearly show the difference between the two sides of the medulla, since on the side contralateral to the lesion of the lemniscus scarcely any nerve cells are to be recognized in the nucleus gracilis and nucleus cuneatus in contrast to the numerous cells to be seen occupying the whole area of the same nuclei of the homolateral side, particularly in both the pars triangularis and the pars rotunda of the nucleus cuneatus. It is true that a certain number of nerve cells have also disappeared in these homolateral nuclei because of the section of some of their axons before crossing, but the remaining cells are numerous enough to be in sharp contrast to those of the contralateral side, where practically all of them have disappeared. The external cuneate nucleus has suffered no damage, and the number of its nerve cells is normal on both sides.

At a higher level the disappearance of the nerve cells in the nucleus cuneatus and remaining portion of the nucleus gracilis contralateral to the lesion of the

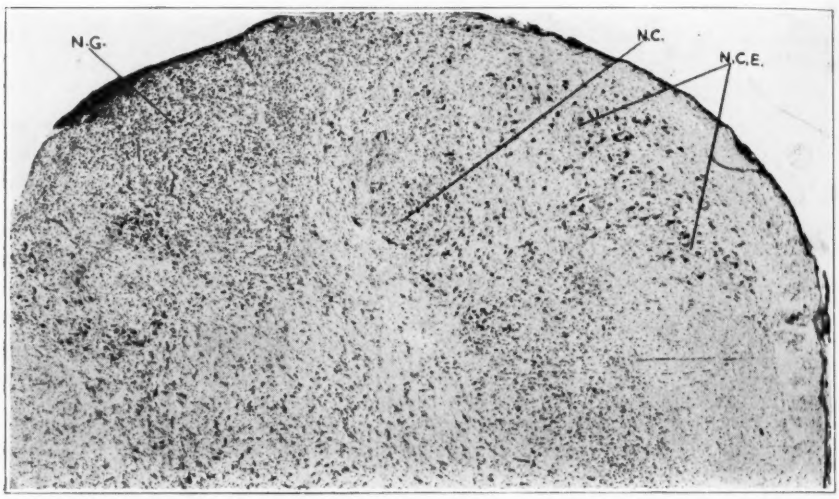


Fig. 6.—From the section of the medulla oblongata of the same animal as in figure 5. The figure illustrates the side contralateral to the normal medial lemniscus. Notice the abundance of nerve cells in the nuclei gracilis and cuneatus contrasting with the absence of nerve cells in the same structures in the contralateral side (fig. 5). *N.C.E.* is the external cuneate nucleus; *N.G.*, the nucleus gracilis, and *N.C.*, the nucleus cuneatus. Nissl stain.

lemniscus is still evident, contrasting with the much better preserved nuclei of the homolateral side. A normal appearance of the external cuneate nucleus is visible on both sides.

Study of serial sections in this case shows also that nerve cells, identical in morphology with those of the external cuneate nucleus, are seen crossing here and there the pars triangularis of the cuneate nucleus as well as at the base of its pars rotunda. Such a persistence of the large nerve cells in the face of the disappearance of the nerve cells of the nucleus gracilis and nucleus cuneatus proper confirms the view expressed in our anatomic survey of the normal structure of these nuclei, namely, that the large cells of the aforementioned bridge as well as the cells accumulated at the base of the pars rotunda are evidently projections of the external cuneate nucleus into the area of the posterior funiculus.

The normal presence of the large nerve cells in the external cuneate nucleus is also a confirmation of different connections established by the nucleus gracilis and nucleus cuneatus and by the nucleus cuneatus externus.

COMMENT

Our experimental work, which in addition to the material reported includes an investigation to be described elsewhere on the termination of the dorsal root fibers in the various cell groups, allows us to bring out the fact that in the posterior funiculus there is in addition to the nucleus gracilis and nucleus cuneatus another important nuclear mass, the structure and function of which is different from that of the two aforementioned nuclei. This cell mass, the existence of which has been considerably neglected by both physiologists and clinicians in interpreting the symptomatology of lesions in the posterior funiculi, has been known under the most various denominations.

In this paper, we have been able to confirm from the morphologic standpoint the fact, already mentioned by Clarke in 1868 [1] and developed later by von Monakow [8] and Blumenau,[9] that the connections of the cells of this nucleus are definitely different from those of the nucleus gracilis and nucleus cuneatus. The bodies of the cells composing the external cuneate nucleus are multipolar and vesicular, and contain well developed nuclei and nucleoli. Their size and form closely resemble those of the cells of Clarke's column. Because of this fact and because of the absence in the cervical region of a definite group of cells homologous to Clarke's column in the thoracic region, the opinion has been advanced that the external cuneate nucleus is the homolog of Clarke's column for the upper extremities.

In another experimental investigation, the result of which will be published separately, we have been able to establish a definite connection between fibers of the fasciculus cuneatus and the external cuneate nucleus.

The ending of fibers of the cervical roots in this nucleus was first experimentally established by von Monakow [10] (1883), who, following lesions of the fasciculus cuneatus in cats and rabbits, pointed out that fibers of this tract end in the external cuneate nucleus. In 1893 Sherrington [11] reported that section of the second right cervical root in

8. von Monakow, C.: Neue experimentelle Beiträge zur Anatomie der Schleife, Neurol. Centralbl. **4**:265, 1885.

9. Blumenau, L.: Ueber die Kerne der Hinterstränge und ueber die Rolando'sche Substanz im verlängerten Mark, Neurol. Centralbl. **15**:1129, 1896.

10. von Monakow, C.: Experimenteller Beitrag zur Kenntnis des Corpus restiforme, des "äusseren Acusticuskerns" und deren Beziehungen zum Rückenmark, Arch. f. Psychiat. **14**:1, 1883.

11. Sherrington, C. S.: Note on the Spinal Portion of Some Ascending Degenerations, J. Physiol. **14**:255, 1893.

Macacus rhesus was followed by ascending degeneration in the lateral cuneate nucleus. In 1897 Thomas [12] reported that, following hemisection of the spinal cord at the level of the second cervical segment in a cat, he was able to follow degenerated fibers of the posterior funiculus into the external cuneate nucleus. In 1932 Ranson, Davenport and Doles,[6] in describing the intramedullary course of the dorsal fibers of the first three cervical roots in cats, were able to follow the ascending degenerated fibers into the same nucleus. In 1933 I. J. Pass,[13] following section of the sixth and seventh cervical roots, described degenerated fibers ascending to the same cell structure.

In our own experimental work,[14] which included isolated sections of the second and third cervical roots, combined section of the first four cervical roots, combined section of the last four cervical roots, section of the first, second and third thoracic roots and section of the third and fourth thoracic roots, we were always able to follow degenerated fibers ending in the external cuneate nucleus. The fibers of the upper cervical roots ending in the external cuneate nucleus occupy the ventral portion of the nucleus, whereas the fibers from the lower cervical and thoracic roots occupy the dorsal segment of the same nucleus.

As the axons of the cells of the external cuneate nucleus are directed toward the cerebellum the situation, therefore, is homologous to that in Clarke's column at lower levels of the spinal cord. The only difference consists in the fact that the number of fibers of the fasciculus cuneatus ending in the external cuneate nucleus is quite considerable, thus making the connections between the cervical roots and the cerebellum more important than the one existing for the trunk and lower extremities.

In addition to the nucleus gracilis and nucleus cuneatus and to the lateral cuneate nucleus, we have been unable to detect other cell groups possessing anatomic as well as functional individuality. We believe, therefore, that the statement of those who speak of a nucleus corporis restiformis in addition to the aforementioned nuclei only adds to an already existing confusion. The nucleus corporis restiformis is nothing but the external cuneate nucleus. We have been unable to distinguish these two in the monkey as has been attempted by some authors. According to them, Monakow's nucleus, being an entirely different structure from the external cuneate nucleus, disappears following hemisection of the cord, whereas the latter nucleus remains intact. In our experimental

12. Thomas, A.: Le cervelet: étude anatomique, clinique et physiologique, Paris, Steinheil, 1897.

13. Pass, I. J.: Anatomic and Functional Relationship of the Nucleus Dorsalis (Clarke's Column), Arch. Neurol. & Psychiat. **30**:1025 (Nov.) 1933.

14. Ferraro, A., and Barrera, S. E.: Posterior Column Fibers and Their Termination in the Posterior Column Nuclei, J. Comp. Neurol., to be published.

material we have been unable, following hemisection of the cord at the level of the second cervical segment, to detect any change in the full length of the external cuneate nucleus, thus establishing the continuity in structure and function of this nucleus.

We also believe that the detailed anatomic division adopted by von Monakow and Fuse [15] in regard to the nuclei of the posterior funiculus is an unnecessary complication, in view of the fact that the various divisions which they create in outline in the external cuneate nucleus and in the cuneate nucleus proper are definitely uncertain. In fact, we have been unable to detect with any degree of certainty the topographic limits between the dorsal and ventral portions of either the cuneate or the external cuneate nuclei reported by these authors. We have also been unable to establish the individuality of the group of cells indicated by von Monakow and Fuse as the nucleus interquintocuneatus, located between the ventral portion of the cuneate nucleus and the spinal root of the fifth nerve.

In addition, we believe that the scattered nerve cells indicated by von Monakow and Fuse as the nucleus interstitialis are nothing but nerve cells belonging to the external cuneate nucleus, which in serial section can be seen connected here and there with the main mass of the nucleus through bridges of scattered nerve cells. Following lesions of the contralateral lemniscus it can be seen that these cells form the medial expansion of the external cuneate nucleus and differentiate themselves from the cells of the nucleus gracilis and nucleus cuneatus, which disappear.

Though a division of the cuneate nucleus into a dorsal and ventral portion is uncertain, we favor the distinction of medial and lateral portions. The medial part is characterized by its roundish appearance which, at higher levels, shows some sort of concentric lamination of cells and fibers and might be called the pars rotunda. The lateral portion, which has the appearance of an isosceles triangle with a ventral base, might be called the pars triangularis. The morphology of the cells in the two parts is somewhat different, the nerve cells of the pars rotunda being larger than those of the pars triangularis. The connections of both parts are the same, since the cells disappear in both portions following lesion of the contralateral medial lemniscus. Among the cells of both the pars rotunda and the pars triangularis are scattered cells the morphology of which is identical with the cells of the external cuneate nucleus.

Following complete removal of the cerebellum or following a section of the inferior cerebellar peduncle we have been able to establish that

15. von Monakow, C., and Fuse, G.: Mikroskopischer Atlas des menschlichen Gehirns: Part I. Die Medulla oblongata, Zurich, Orell Füssli, 1916, tables IIa, IIb and III.

the majority of the cells of the external cuneate nucleus disappear, in contrast to the persistence of nerve cells in the nucleus gracilis and nucleus cuneatus. Following removal of the cerebellum there is also disappearance of most of the large nerve cells which we have previously mentioned and which are found scattered here and there at the base of the pars rotunda of the cuneate nucleus and among the cells of its triangular portion. There are, however, a few cellular elements which still remain in the external cuneate nucleus but which appear deeply stained and shrunken. We are inclined to believe that these cells also send their axons toward the cerebellum but that their disappearance has not taken place for reasons which are not clear, one of them at least being that one is dealing with adult animals. It might be contended that these cells give origin to axons which contribute to the formation of the medial lemniscus instead of the inferior cerebellar peduncle. However, to favor such an interpretation we should have found a tangible disappearance of nerve cells of the external cuneate nucleus following a lesion of the medial lemniscus, which fact we are hesitant to admit.

While cells of the external cuneate nucleus disappear following section of the inferior cerebellar peduncle, we found no such loss of cells following hemisection of the cord. We are therefore unable to confirm von Monakow's data on the subject. In fact, we think, as already mentioned, that the original report of von Monakow regarding the disappearance of nerve cells in the external cuneate nucleus (since then, often called the nucleus of Monakow) as well as the acceptance of such data by the majority of authors is entirely misleading. We have, in fact, gone over the original work of von Monakow and we are under the impression that in his experiment of hemisection of the cord at a very high level, he must have injured directly the external cuneate nucleus, which injury resulted in a cicatricial process in the nucleus itself, followed by the disappearance of a considerable number of nerve cells. Such a disappearance was interpreted by von Monakow as the result of section of axons directed from the nucleus toward the spinal cord.

Finally, following destruction of the medial lemniscus we have been able to establish that the nerve cells of the nucleus gracilis and nucleus cuneatus disappear, whereas the cells of the external cuneate nucleus remain intact.

Our anatomic and experimental investigations have therefore established the existence in the posterior funiculus of three different groups of cells. Two of these, the nucleus gracilis and nucleus cuneatus, contribute mainly to the formation of the lemniscus medialis, and undergo atrophy when the lemniscus is damaged. The third group, the external

cuneate nucleus, undergoes atrophy when the inferior cerebellar peduncle is sectioned. It therefore probably supplies important connections to the cerebellum.

CONCLUSIONS

1. An anatomic study of the cell groups of the posterior funiculus is made in Macacus rhesus. As a result of such a survey it has been established that there are three main nuclei: (*a*) the nucleus gracilis, (*b*) the nucleus cuneatus and (*c*) the external cuneate nucleus.

2. The nucleus cuneatus is divided into a medial portion or pars rotunda and a lateral portion or pars triangularis.

3. Following lesions of the medial lemniscus the cells of the nucleus gracilis and nucleus cuneatus in both the pars rotunda and pars triangularis disappear, whereas the cells of the external cuneate nucleus remain intact.

4. Following removal of the cerebellum or simple section of the inferior cerebellar peduncle the cells of the external cuneate nucleus disappear on the same side as the lesion, whereas the cells of the nucleus gracilis and nucleus cuneatus remain intact.

5. Following hemisection of the spinal cord no changes of appreciable value are noticeable in any of the aforementioned groups of cells in the posterior funiculus.

6. It follows, therefore, that the connections of the nucleus gracilis and nucleus cuneatus are different from the connections of the external cuneate nucleus.

7. The axons of the cells of the nucleus gracilis and nucleus cuneatus are sent into the medial lemniscus, whereas the axons of the cells of the external cuneate nucleus are sent to the cerebellum via the inferior cerebellar peduncle of the same side.

8. In the external cuneate nucleus no anatomic division can be experimentally established between the oral and the caudal portions (the latter, the "spinal portion" of some authors).

9. The cell groups known as the nucleus interquintocuneatus and the nucleus interstitialis of von Monakow and Fuse seem to represent only medial projections of the external cuneate nucleus.

10. The connections between the cervical and high thoracic posterior roots and the external cuneate nucleus are discussed and experimental data are summarized to establish such connections. The importance of the cerebellar element in lesions of the posterior funiculi of the cervical and high thoracic segments is therefore brought forward from both the physiologic and the clinical standpoint.

CEREBRAL CIRCULATION

XXXV. THE COMPARATIVE EFFECT OF ERGOTAMINE TARTRATE ON THE ARTERIES IN THE PIA, DURA AND SKIN OF CATS

J. L. POOL, M.D.

AND

G. I. NASON, M.S.

BOSTON

Owing to the fact that ergotamine tartrate [1] has been found to be one of the most effective substances in the treatment of the headache of migraine, a series of experimental studies has been undertaken with a view to obtaining more information concerning the mechanism by which relief is afforded. In this article we shall deal only with the experimental results found and a discussion of these observations with respect to the pain of migraine. For further discussion of ergotamine tartrate, we refer to related studies [2] which summarize its physiologic action and describe its therapeutic effects.

The effect of ergotamine on the pial vessels was studied not only because of the paucity of information on the subject, but also because of the theory reviewed by Riley,[3] Robey [4] and others that vasospasm may be one of the important factors in the production of the symptoms of a migraine attack. On this theory, that a sympatheticodepressant might be expected to cause relaxation of such a "spasm," ergotamine was employed in the treatment of migraine.[2]

The dural vessels were also studied in view of the probable relation between meningeal vessels and headache which has been pointed out by Cushing [5] and other writers.

This work was aided by a grant from the Josiah Macy Jr. Foundation.

From the Department of Neuropathology, Harvard Medical School, and the Neurological Unit, Boston City Hospital.

1. The ergotamine tartrate used in these experiments was supplied by the Sandoz Chemical Works, Inc., New York.

2. Lennox, W. G.: The Use of Ergotamine Tartrate in Migraine, New England J. Med. **210**:1061, 1934. Pool, J. L.; von Storch, T. J. C., and Lennox, W. G.: The Effect of Ergotamine Tartrate on the Cerebrospinal Fluid and Blood Pressure of Patients During Migraine Headache, Arch. Int. Med., to be published.

3. Riley, H. A.: Migraine, Bull. Neurol. Inst. New York **2**:429, 1932.

4. Robey, W. H.: Headache, Philadelphia, J. B. Lippincott Company, 1931.

5. Cushing, H., in Keen, W. W.: Surgery: Its Principles and Practice, Philadelphia, W. B. Saunders Company, 1908, vol. 3, p. 160.

PROCEDURE

Healthy young cats weighing between 2 and 5 Kg. were anesthetized with an intraperitoneal injection of a 1 per cent solution of amytal (7 cc. per kilogram of body weight). An electric heating pad was employed to maintain the animal's body temperature.

A cranial window [6] was screwed into the skull, permitting direct microscopic observation and measurement of the underlying pial vessels. Observations on the vessels of the dura mater were made in a similar fashion,[7] as well as microscopic measurements of the peripheral arteries (skin of the ear [8] and a forelimb).

The systemic blood pressure and cerebrospinal fluid pressure were recorded in the usual manner: A cannula was inserted into the femoral artery and connected with a mercury manometer; a needle was introduced into the cisterna magna and connected with a manometer of 1 mm. bore filled with Ringer's solution. Venous pressure was obtained on several occasions by inserting a cannula into the subclavian vein at its junction with the external jugular vein. Records of the pulse rate were obtained by frequent counts of the cardiac impulse as reflected in the sphygmomanometer.

Ergotamine was administered intravenously on all but a few occasions when the effect of intracarotid injection was tested (as noted), the injection at such times being made into the artery on the same side of the head as the cranial window. The effect of a variety of dosages was studied: (1) a small dose corresponding to the human equivalent, i. e., from 0.0037 to 0.007 mg. per kilogram of body weight, which it was felt represented a close approach to the physiologic dose and (2) larger doses of from 0.007 to 0.16 mg. per kilogram. The drug was never given unless a preliminary base-line for arterial dimensions, blood pressure and cerebrospinal fluid pressures were determined for at least three (usually five or more) minutes.

RESULTS

A summary of results, compiled from the individual protocols, is given in figure 1.

1. *Effect of Ergotamine on Pial Vessels.*—The arteries of the pia mater were observed (in nineteen cats) after twenty-nine intravenous injections of ergotamine (from 0.0037 to 0.16 mg. per kilogram). The results were inconstant. In approximately one third of the cases the artery did not change in diameter; in one third it constricted, and in one third it dilated. The vascular response did not seem to depend on the dosage, the original size of the vessel or changes in the blood pressure or spinal fluid pressure. The effect of intracarotid administration cannot surely be ascribed to the action of the ergotamine itself, since it is put up

6. Forbes, H. S.: The Cerebral Circulation: I. Observation and Measurement of Pial Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

7. Pool, J. L.; Nason, G. I., and Forbes, H. S.: The Cerebral Circulation: XXXIII. The Effect of Nerve Stimulation and Various Drugs on the Vessels of the Dura Mater, Arch. Neurol. & Psychiat. **32**:1202 (Dec.) 1934.

8. Forbes, H. S.; Finley, K. H., and Nason, G. I.: The Cerebral Circulation: XXIV. C. Vasomotor Response in the Pia and in the Skin, Arch. Neurol & Psychiat. **30**:970 (Nov.) 1933.

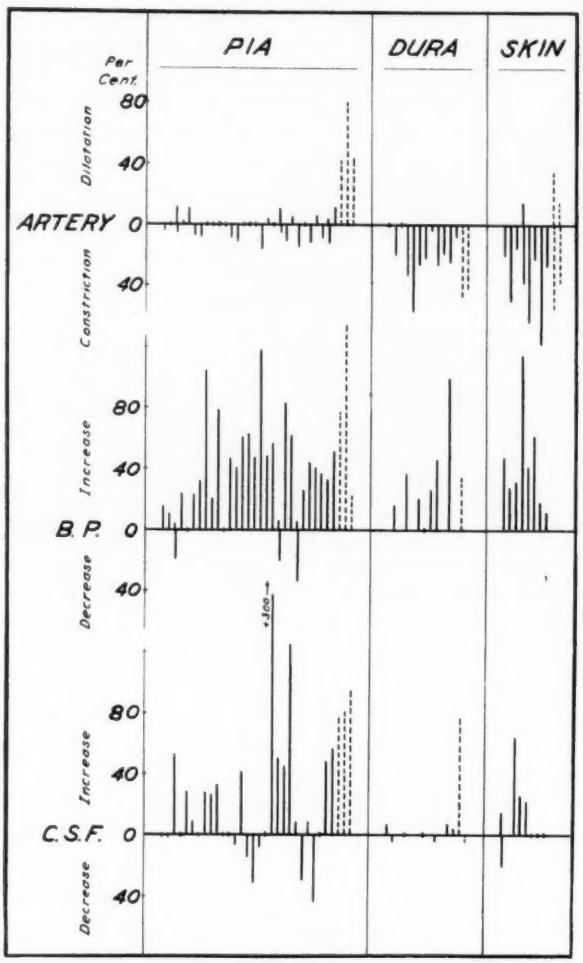


Fig. 1.—The lines represent the percentage changes in the diameter of the artery, in the blood pressure and in the cerebrospinal fluid pressure in each experiment; the changes of each in a single experiment are directly beneath one another. Also the experiments in each group (pia, dura and skin) are arranged in the order of dosage, the dosage increasing from left to right and ranging in the pia group from 0.0037 to 0.16 mg. per kilogram, in the dura group from 0.012 to 0.119 mg. per kilogram and in the skin group from 0.0100 to 0.0677 mg. per kilogram. The solid lines represent intravenous injections and the broken lines intracarotid injections.

in acid solution as a means of preservation, acid being capable of producing pial vasodilatation.[9]

2. Effect of Ergotamine on Dural Vessels.—In contrast with the arteries of the pia, those of the dura constricted following the intravenous or intracarotid injection of ergotamine (from 0.012 to 0.119 mg. per kilogram). In fourteen trials (on ten cats) a significant change in diameter occurred twelve times, the average constriction in these twelve trials being 25 per cent. Usually a simultaneous slowing of both venous and arterial flow was observed. It is of interest to note that after ergotamine the blood pressure often remained elevated for an appreciable period (from ten to twenty minutes) after the constricted dural artery had returned to its original size.

In view of the fact that ergotamine has been found to depress sympathetic activity and reverse the customary effects of epinephrine

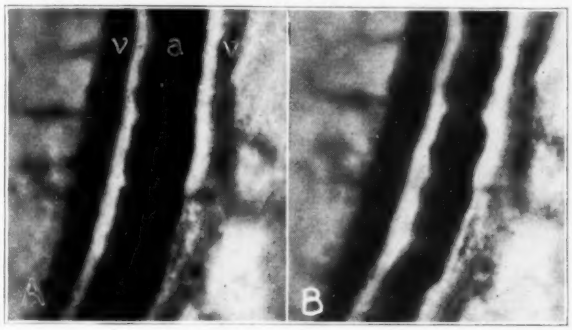


Fig. 2.—Photomicrographs (high power) of dural vessels taken with a Leica camera, Persenso film. *A* is the control; *B* was taken eighty-five seconds after the intravenous injection of 0.25 mg. of ergotamine tartrate (0.10 mg. per kilogram); *a* indicates the dural artery, on either side of which lie the venae comites (*v*). The irregularities in the constricted vessel were due in this instance to some degree of previous trauma and are not characteristic of the effect of ergotamine.

(Rothlin [10] and others), it is of interest that in the three experiments in which stimulation of the sympathetic nerve followed the administration of ergotamine, the dural artery constricted only from one fourth to one third as much as it had done under the same stimulation previous to the injection of ergotamine. The artery had regained its original diameter before sympathetic stimulation was begun, the lessened

9. Wolff, H. G., and Lennox, W. G.: The Cerebral Circulation: XII. The Effect on Pial Vessels of Variations in the Oxygen and Carbon Dioxide Content of the Blood, Arch. Neurol. & Psychiat. **23**:1097 (June) 1930. Forbes, H. S., and Krumbhaar, C. C.: The Cerebral Circulation: XXI. Action of Hydrogen Sulphide, Arch. Neurol. & Psychiat. **29**:756 (April) 1933.

10. Rothlin, E.: The Specific Action of Ergot Alkaloids on the Sympathetic Nervous System, J. Pharmacol. & Exper. Therap. **36**:657, 1929.

response being due presumably to partial paralysis of the sympathetic nerve endings. Furthermore, in the two experiments in which epinephrine was given after ergotamine, a moderate constriction (17 per cent) ensued once and a dilatation once, this being the only occasion when epinephrine was followed by dilatation.

3. *Peripheral Vessels (Skin).*—The arteries of the skin also constricted strongly following the intravenous injection of ergotamine. In seven of eight trials a constriction occurred, the average decrease in diameter being 39 per cent. Once there was a dilatation followed by constriction. Two intracarotid injections also resulted in a dilatation followed by constriction. This vasoconstriction in both skin and dura is due presumably to local stimulation of the muscular coats of the arteries, for unless such action did occur, the paralysis of sympathetic nerve endings by ergotamine should cause dilatation. A generalized peripheral vasoconstriction might explain the rise in arterial pressure after ergotamine, also the changes in venous and, consequently, in cerebrospinal fluid pressure by the mechanism just described. Furthermore, the variability in the reaction of the arteries in the pia may be explained by supposing that ergotamine exerts a feeble constrictor action on these vessels which may be counteracted or overshadowed by a passive dilatation secondary to a rise of blood pressure.

4. *Blood Pressure.*—The effect on the blood pressure proved fairly constant, for regardless of the mode of administration or the dosage, an elevation was noted in forty-two of forty-eight experiments, no change three times and elevation followed by immediate fall, three times.

5. *Cerebrospinal Fluid Pressure.*—In forty-eight experiments, elevation of the cerebrospinal fluid pressure followed the administration of ergotamine twenty-five times, elevation with a subsequent fall once, no change thirteen times and a fall in pressure nine times. It may be inferred, therefore, that the general tendency of ergotamine is to produce elevation or no change in the spinal fluid pressure.

6. *Venous Pressure.*—Elevation occurred on four occasions, no change three times and a fall once, these changes in general paralleling those of the spinal fluid pressure. Since the pressure of the cerebrospinal fluid depends primarily on the venous pressure,[11] these findings are not unexpected. Venous pressure, depending largely on the ratio of blood volume to the volume of the vascular bed, may be altered by the peripheral vasoconstriction following ergotamine.

---

11. Fremont-Smith, F., and Kubie, L. S.: Relation of Vascular Hydrostatic Pressure and Osmotic Pressure to Cerebrospinal Fluid Pressure in Intracranial Pressure in Health and Disease, Association for Research in Nervous and Mental Disease, ser. research pub., vol. 8, p. 104, Baltimore, Williams & Wilkins Company, 1929.

7. Pulse Rate.—The pulse rate was observed before and after injection twenty times, all changes in rate taking the form of a decrease (80 per cent of the cases).

COMMENT

Many observers have pointed out that the traction or ligation of the meningeal arteries during surgical procedures on man is capable of producing pain, Cushing,[5] in 1908, having made the following statement: "It is my impression that most headaches—those of the migrainous, as well as of other types—are largely dural in origin." Acting on these suggestions, Dickerson [12] operated on seven patients suffering from headaches (migrainous, traumatic, etc.) and ligated the middle meningeal artery. He reported striking relief of headache on the side operated on. Insufficient time has elapsed, however, and the number of cases is too small to permit one to draw definite conclusions as to the value of this procedure. It has been suggested by Hare,[13] furthermore, that the dilatation of dural vessels may be responsible for migraine headaches, as compression of the carotid artery on the affected side may diminish the pain, and pressure on the contralateral carotid may increase it. It has also been pointed out that drugs like amyl nitrite and glycerol trinitrate which produce a feeling of "fulness in the head," or a severe throbbing headache,[14] also dilate the intracranial vessels.[15] Pickering [16] analyzed still further the relationship between headache, dural perivascular innervation and vasodilation.

The accumulated evidence suggests that the dilatation of dural arteries is closely connected with various types of headache, including migraine. Experiments reported here show that in cats the dural arteries are constricted by ergotamine tartrate. It is suggested that the mechanism by which this drug affords relief from the headache in migraine may be associated with the constriction of these vessels.[2]

SUMMARY

A. The effects of the intravenous administration of ergotamine tartrate on anesthetized cats may be summarized as follows: (1) incon-

12. Dickerson, D. G.: Surgical Relief of the Headache of Migraine, J. Nerv. & Ment. Dis. **77**:42, 1933.

13. Hare, F.: The Mechanism of Pain in Migraine, M. Press & Circ. **130**:23, 1905; quoted by Riley.[3]

14. Leake, C. D.; Loevenhart, A. S., and Muehlberger, C. W.: Dilatation of Cerebral Blood Vessels as Factor in Headache, J. A. M. A. **88**:1076 (April 2) 1927.

15. Wolff, H. G.: The Cerebral Circulation: XI. C. The Action of Amyl Nitrite, Arch. Neurol. & Psychiat. **22**:695 (Oct.) 1929.

16. Pickering, G. W.: Observation on the Mechanism of Headache Produced by Histamine, Clin. Sc. **1**:77, 1933.

stant effects on the caliber of the pial arteries; (2) constriction of the dural arteries, the average decrease in diameter being 25 per cent; (3) constriction of the arteries of the skin (average 39 per cent); (4) elevation of the systemic arterial pressure; (5) elevation or no change in the cerebrospinal fluid pressure; (6) alteration in the venous pressure similar to that of the cerebrospinal fluid pressure; (7) decrease in the pulse rate.

B. Evidence from various sources suggests that the headache of migraine may be caused, in part, by the dilatation of the arteries in the dura.

CONCLUSION

On the basis of the experiments on animals here reported it is suggested that the clinical relief of the headache of migraine by the administration of ergotamine may be related to dural vasoconstriction.

Of special interest is the difference in effect of ergotamine on the arteries in the pia, the dura and the skin.

SACROCOCCYGEAL CHORDOMAS

A CLINICAL AND PATHOLOGIC STUDY

ELEANOR M. FLETCHER, M.D.
Fellow in Pathology, the Mayo Foundation

HENRY W. WOLTMAN, M.D.

AND

ALFRED W. ADSON, M.D.

ROCHESTER, MINN.

A chordoma is a tumor which arises from remnants or "rests" of the embryonic notochord. It is found almost exclusively in two positions in the body, the clivus Blumenbachii and the sacrococcygeal region. In the latter position the tumor may arise in the sacrum and remain there for the most part, it may grow into the pelvis with the formation of a presacral tumor or it may grow posteriorly, giving rise to a postsacral tumor. The sites of origin are the notochordal remnants found normally in the nuclei pulposi of the sacrum, and possibly heterotopic foci of chordal tissue anterior or posterior to the sacrum. In this article the clinical manifestations, the surgical treatment and the histopathologic observations in ten new cases of sacrococcygeal chordoma are presented, together with a brief survey of the more important literature.

It is interesting that all the earlier cases of chordoma reported occurred in the region of the clivus Blumenbachii. The first case of sacrococcygeal chordoma was observed in 1910 by Feldmann,[1] who removed a presacral tumor the size of an apple from a woman, aged 46. This tumor had no definite attachment to the sacrum.

In 1919 Pototschnig [2] reported an extremely large presacral chordoma, weighing 13 pounds (5.9 Kg.). This tumor was of ten years' duration and at necropsy was found to have invaded the regional lymph nodes and the liver. In 1921, Lewis [3] described four cases, in three of which there was widespread metastasis. In 1922, Stewart [4] reviewed

---

From the Sections on Neurology (Dr. Woltman) and Neurologic Surgery (Dr. Adson), the Mayo Clinic.

Read before the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 4, 1934.

1. Feldmann, I.: Chordoma ossis sacri, Beitr. z. path. Anat. u. z. allg. Path. **48**:630, 1910.

2. Pototschnig, G.: Ein Fall von malignem Chordom mit Metastasen, Beitr. z. path. Anat. u. z. allg. Path. **65**:356, 1919.

3. Lewis, N. D. C.: A Contribution to the Study of Tumors from the Primitive Notochord, Arch. Int. Med. **28**:434 (Oct.) 1921.

4. Stewart, M. J.: Malignant Sacrococcygeal Chordoma, J. Path. & Bact. **25**:40, 1922.

the previously reported cases of clinical interest and described a case of his own in which a detailed histologic study was made.

A comprehensive review of the entire subject of chordomas was published by Coenen [5] in 1925. In 1926 Stewart and Morin [6] described a case of sacrococcygeal chordoma in which a clinical diagnosis had been made and confirmed histologically. At that time Stewart set forth the criteria by which the histologic diagnosis of chordoma can be made.

Andler,[7] also in 1926, contributed to the literature a comprehensive review of sacrococcygeal chordomas which was primarily of clinical interest. Since 1926 many other similar sacrococcygeal chordomas have been reported, while complete reviews of the literature have been given by Machulko-Horbatzewitsch and Rochlin [8] and by Fletcher.[9]

REPORT OF CASES

CASE 1.—For two years, a farmer, aged 33, had been suffering from constipation and from a steadily increasing pain at the lower end of the spine. Four weeks before registration, on July 12, 1910, an operation for hemorrhoids had been performed. Two weeks later, at a second operation for the same purpose, a tumor had been discovered.

Digital examination disclosed a presacral tumor. No neurologic examination was made, but the records showed that the patellar and achilles reflexes were normal.

On July 14 the tumor was removed by a modified Kraske procedure. This was followed by administration of Coley's serum and the application of radium.

On Dec. 8, 1911, the patient reported that his condition had improved in every way. He had gained 25 pounds (11.3 Kg.). He had experienced occasional pain in the sacral region, which had lasted from one minute to two hours, about once a week. A tumor lying within the pelvis was palpable.

On Sept. 5, 1917, he said that there was some numbness along the posterior aspect of the right thigh and of the foot and that for three weeks he had found it necessary to empty his bladder by catheter. On rectal examination, an extensive mass, which extended upward into the left side of the pelvis, was palpated.

The man died on May 18, 1919, eleven years after the onset of symptoms and nine years after operation and treatment with Coley's serum and radium.

The tissue was made up of lobules of tumor cells separated from each other by narrow strands of connective tissue (fig. 1). At the periphery of the lobules the tumor cells were large and irregularly polygonal in shape, with distinct outlines, and were arranged to form a solid sheet of cells. The majority of the cells contained a few vacuoles in their basophilic cytoplasm. In some the vacuolation

5. Coenen, Hermann: Das Chordom, Beitr. z. klin. Chir. **133**:1, 1925.

6. Stewart, M. J., and Morin, J. E.: Chordoma: A Review, with Report of a New Sacrococcygeal Case, J. Path. & Bact. **29**:41, 1926.

7. Andler, Rudolph: Die Klinik des sacrococcygealen Chordoms, Arch. f. klin. Chir. **143**:467, 1926. Andler, Rudolph, and Schmincke, A., quoted by Stewart.[4]

8. Machulko-Horbatzewitsch, G. S., and Rochlin, L. L.: Klinik, Pathomorphologie, und Histogenese der Chordome, Arch. f. Psychiat. **89**:222, 1930.

9. Fletcher, Eleanor M.: Thesis, University of Minnesota, December 1933.

Fig. 1.—Lobule of tumor cells with the characteristic radial arrangement of the cords of cells. The interlobular stroma is represented. Hematoxylin and eosin; × 80.

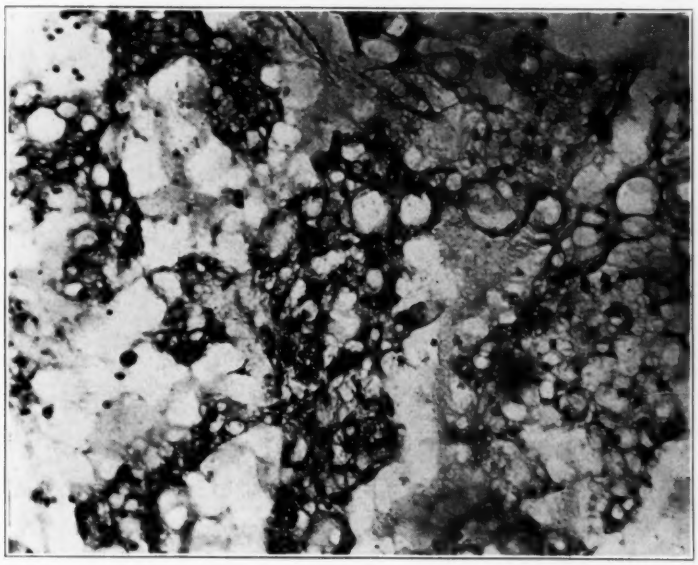


Fig. 2.—A typical area with the vacuolated physaliphorous cells and intercellular mucus. Hematoxylin and eosin; × 185.

was so extreme that typical physaliphorous cells were produced, while in others the nuclei of the cells were displaced to one side and flattened by one large vacuole. Many of the vacuoles contained a homogeneous, faintly basic staining material, while the remainder appeared to be empty. The nuclei of the cells were vesicular and stained poorly, and a few of them contained vacuoles. In the larger cells, prominent nucleoli were present, and a few multinucleated cells were observed, but mitotic figures could not be found in any of the cells.

In the central lobular regions the tumor cells, instead of being closely packed together, were arranged radially in cords or in small groups widely separated by a homogeneous, intercellular substance which appeared to be of the same nature as the content of the cytoplasmic vacuoles. The tumor cells were small and cuboidal, with eosinophilic cytoplasm and small, shrunken, deep-staining nuclei. Small cytoplasmic vacuoles were present in some of the cells (fig. 2). These areas of the neoplasm closely resembled the embryonic notochord as seen in the nuclei pulposi of intervertebral disks.

The stroma of the tumor was dense fibrous connective tissue which in some situations had undergone extensive hyalinization. Collections of lymphocytes, plasma cells and eosinophilic leukocytes surrounded some of the thin-walled blood vessels.

In sections stained with mucicarmine it was noted that some of the vacuoles contained thick mucus. In the intercellular substance, which was abundant toward the centers of the lobules, the reaction was also positive. The nuclear vacuoles, on the other hand, remained unstained.

Histologically, this tumor presented the characteristic features of a chordoma, as formulated by Stewart in 1926. Its high degree of differentiation was evidenced by the large number of vacuolated tumor cells and the presence of considerable amounts of extracellular mucus. The epithelial-like aspect of the younger and more cellular portions of the tissue was absent in the central lobular zones, where the resemblance to notochordal tissue left little doubt as to the true nature of the tumor.

Case 2.—A farmer, aged 68, registered as a patient at the Mayo Clinic on April 27, 1916, because of intense nocturnal pain in the distribution of the left sciatic nerve. One month previously he had been operated on for hemorrhoids. For two weeks he had had difficulty in voiding urine.

On examination small hemorrhoids were found and a fluctuating sacral tumor was palpated, which had partially destroyed the sacrum, as shown by roentgenograms. A "notochord tumor" was suggested as a possibility by Dr. H. S. Plummer. A neurologic examination was not made.

On November 28 a gelatinous tumor of the sacrum and rectum was removed by the Kraske method.

The patient died on Jan. 2, 1918, thirteen months after the operation.

Microscopic examination of the tumor revealed that it had a definite lobular arrangement similar to that described in case 1. The tumor cells varied considerably in size, and typical physaliphorous cells were frequently observed (fig. 3).

Most of the cytoplasmic vacuoles contained a homogeneous, basic-staining substance which appeared to be similar in nature to the substance present in the intercellular spaces, both of which gave a positive reaction for mucus with the mucicarmine stain. Nuclear vacuoles were not observed, and mitotic figures were not found. Histologically, this tumor was a typical chordoma.

Case 3.—A housewife, aged 43, was delivered of a baby on Jan. 20, 1920. Two or three months later, for one week, there was daily bleeding from the

rectum. In August, pain in the vagina and coccyx and dysuria appeared and led the patient to consult a physician. He discovered a soft, fluctuating mass situated anterior to the sacrum. On incision of the mass through the vagina, about 250 cc. of grumous material was discharged. The physician appreciated that he was dealing with a degenerating tumor. On October 20 the patient was registered at the Mayo Clinic.

On rectal examination, a hard, nodular mass, lying over the left side of the sacrum was palpated. Roentgenograms gave negative results. A neurologic examination was not made.

After removal of an encapsulated tumor on October 25 a course of roentgenotherapy was instituted. The patient died on December 17.

Microscopic examination disclosed that the parenchyma of the tumor was composed of masses of cells with a lobular arrangement. In some portions, the

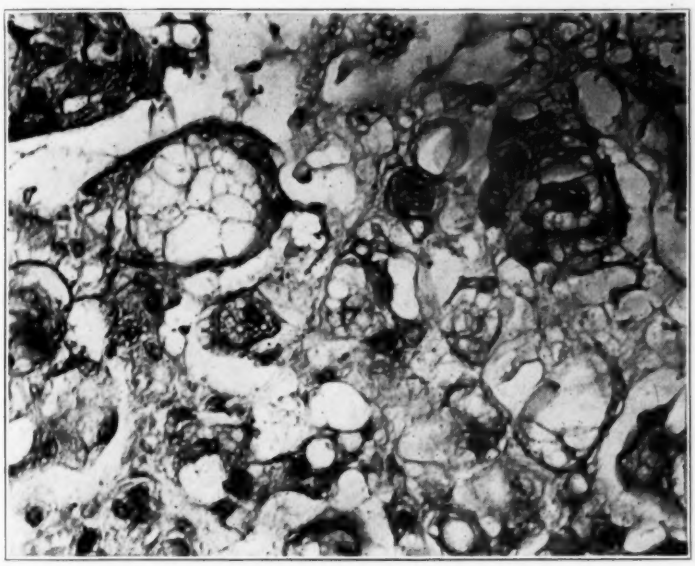


Fig. 3.—A group of physaliphorous cells containing many vacuoles. Hematoxylin and eosin; × 250.

appearance was that of a typical chordoma, similar to that in cases 1 and 2. In other portions the tumor cells presented quite a different appearance; the outlines were indistinct, and the deeply basophilic cytoplasm was scanty. With high magnification commencing vacuolation of these cells could be seen, and tiny collections of a colloid-like substance were present between some of the cells. The nuclei were large and vesicular and contained one or more prominent nucleoli but no vacuoles. Mitotic figures were of frequent occurrence, and many of them were atypical (fig. 4).

The stroma of the tumor was cellular and loosely arranged. It contained many thin-walled blood vessels, but there was no evidence that the tumor had extended into the vascular channels. With the mucicarmine stain small amounts of mucus were found intracellularly throughout the more active parts of the tumor.

This tumor presented an extremely interesting histologic picture in that it contained portions where there was marked lack of differentiation, as well as portions which were well differentiated. The presence of physaliphorous cells containing intracellular mucus was the chief factor on which the diagnosis of chordoma was based. In the more active cellular areas the cells had an epithelial appearance, since they were packed close together, without appreciable intercellular substance or stroma, but there was no evidence of glandular formations in any portion of the tumor. The appearance thus produced was that of a highly malignant neoplasm of which the true nature was exhibited only by a relatively small number of the cells.

CASE 4.—A housewife, aged 25, came to the Mayo Clinic on Nov. 20, 1920, because of pain in the distribution of the right sciatic nerve. At the age of 13, she had fallen on the ice and for four or five years thereafter had suffered from

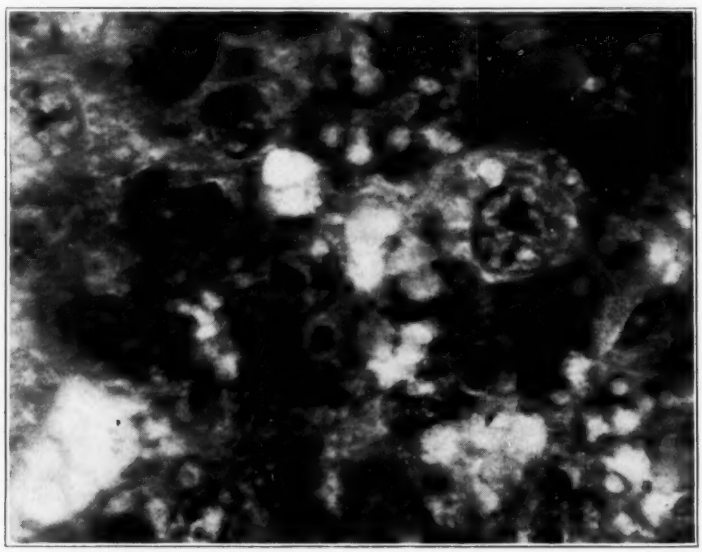


Fig. 4.—A malignant chordoma. A mitotic figure is seen on the left. The cytoplasmic vacuoles and small globules of intercellular mucus can be seen. Hematoxylin and eosin; × 890.

pain in the coccygeal region. At this age, also, migrainous headaches and epileptiform convulsions had put in their appearance. At first the latter had come monthly, later, twice yearly. In July 1918, during the last three months of pregnancy, she had begun to suffer from pain in the region of the right hip and anterior tibial crest. The pain had taken on a dull, boring character, had become continuous, and gradually had included the lumbar region and the entire right sciatic distribution. It had been aggravated by jarring and by lying down, so that she had acquired the habit of sleeping while lying forward over a table, with the knees resting on a chair. For two months she had been incontinent of urine and feces, and during this period both lower extremities had become swollen.

On examination, the lumbar portion of the spine was rigid and tender. Both patellar and achilles reflexes were absent. The anal reflex likewise was absent.

Lasègue's sign was marked on the right. Cutaneous sensation was diminished over the distribution of the right fifth lumbar and first and second sacral segments; it was completely lost below this segmental distribution on the right, and on the left it was lost over the distribution of the fourth and fifth sacral nerves. Nonne's test of the spinal fluid was positive. Roentgen examination of the spine gave negative results.

On Nov. 30, 1920, a tumor that invaded bone and lumbar muscles from the level of the second lumbar to the first sacral vertebrae was partially removed.

On December 27 examination disclosed pronounced weakness of the right lower extremity and slight weakness of the left. The left patellar and achilles tendon reflexes had returned. There was complete anesthesia in the distribution of both right and left second, third, fourth and fifth sacral nerves.

The patient returned on Jan. 13, 1923. Convalescence from the operation had been slow, but she soon became comfortable. Two months before she returned, pain had appeared in the distribution of the left sciatic nerve. On examination, slight weakness of the right lower extremity was noted; power in the left leg was practically normal. An unexpected finding was a sensory disturbance almost identical with that noted at the first examination, save that the sides were reversed. Roentgen therapy was instituted.

The patient died on Oct. 27, 1924, six years after the onset of symptoms and four years after operation.

The tumor was made up of poorly circumscribed masses of neoplastic cells, separated by thick strands of fibrous connective tissue. The tumor cells were cuboidal and were arranged in cords and small groups widely separated by a homogeneous, intercellular substance. Practically all the cells contained one or more cytoplasmic vacuoles, some of which were filled with colloid-like material. When a large number of intracellular vacuoles were present, a honey-combed appearance of the cytoplasm, typical of the physaliphorous cells, was produced. The vesicular nuclei did not contain vacuoles, and mitotic figures could not be found. The content of the cytoplasmic vacuoles and of the intercellular substance gave a positive reaction for mucus. In many portions, throughout the intercellular substance, rounded masses of mucus were formed. These appeared to have been produced by deposition in successive layers, since their concentric nature was prominent. This tumor was a typical example of a well differentiated chordoma; the only unusual features were the mucus concretions, which slightly resembled corpora amylacea.

CASE 5.—For two and a half years, a grocer, aged 47, had suffered from a dull, constant, intense pain which, during the previous four months, had extended down the distributions of both sciatic nerves, more on the right than on the left. For one and a half years the buttocks had been numb, and soon thereafter catheterization had become necessary; the bowels had been under poor control, and for six months impotence had supervened. Occasionally small amounts of blood had escaped from the rectum. The patient registered at the Mayo Clinic on Dec. 27, 1920.

Absolute anesthesia was present in the distribution of the fourth and fifth sacral nerves. A firm, globular, fixed mass, 10 cm. in diameter, was palpated over the anterior surface of the sacrum. Varicose veins were present in both legs. Roentgen examination of the lumbar and sacral portions of the spinal column gave negative results.

On Jan. 3, 1921, exploration for a tumor was made through an abdominal incision. On January 17 a modified Kraske technic was employed to remove as much of the tumor as possible. This was followed by roentgen therapy.

In a communication dated September 1924 we were informed that the patient had died, but the date of death was not given.

This tumor presented an unusual microscopic picture. It appeared to be made up almost entirely of large lobules of peculiar, lacelike structure. This structure was due partly to the extreme vacuolation of the tumor cells and partly to the large amount of vacuolated intercellular substance. A few of the cytoplasmic vacuoles contained a thin, structureless substance which gave a positive reaction for mucus, but the majority appeared to be empty. There was no evidence of nuclear vacuolation, and mitotic figures could not be found.

The histologic features characteristic of a chordoma were presented by this tumor. The extreme vacuolation of the tumor cells and the large amounts of extracellular mucus formed an excellent example of the extent to which the production of mucus can go in some tumors belonging to this group.

CASE 6.—A housewife, aged 65, registered at the Mayo Clinic on Sept. 4, 1923, giving as her chief complaint pain in the rectum and in the distribution of both sciatic nerves. When she was 19, some one had pulled a chair from under her; this had resulted in a fall and pain in the coccygeal region for two weeks. In 1918 pain in the coccygeal region had again made its appearance. There had been tenderness, and the pain had been made worse by jarring and by movement of the bowels. In 1920 hemorrhoids had been discovered and operated on; the procedure had not alleviated the pain but had resulted in a loss of control of the anal sphincter. Three months later, injection of alcohol into the nerves had been equally ineffective; two weeks after the injection the coccyx had been successfully removed, but without noticeable benefit to the patient. In February 1922 she had been incontinent of feces for three months, and in January 1923 this condition had reappeared, to remain.

On examination the patient walked cautiously because of the pain. Bending backward was also painful. The anal sphincter was patulous, and on rectal examination a tender mass was palpated over the anterior part of the sacrum. In the distribution of the fourth and fifth sacral nerves, sensations of touch, pain and temperature were moderately impaired. Nonne's reaction of the spinal fluid was positive. Roentgenograms of the sacrum disclosed destruction of the first, second and third sacral vertebral bodies.

On Oct. 6, 1923, a pulpy, hemorrhagic tumor was removed as completely as possible.

In a letter received on March 29, 1926, the patient's physician reported that he thought the patient had died.

Microscopically, this tumor was a typical chordoma, in which there was well marked differentiation. Nuclear vacuoles were present but did not give a positive reaction for mucus. Mitotic figures were not found in any portion of the tumor.

CASE 7.—A retired banker, aged 47, came to the Mayo Clinic on July 28, 1924, because of rectal pain. Two months previously a sensation of numbness had made its appearance in the anal and coccygeal regions. One month later this had been followed by a steady, dull, boring pain in the rectum, radiating slightly into the gluteal regions. Coughing had not aggravated it. It had occurred only at night and had permitted sleeping in shifts of one or two hours only, so that the man had often sought comfort several times each night by leaving his bed and walking around.

Examination disclosed a slight rigidity of the lumbosacral portion of the spinal column. A slight impairment of all superficial sensibility was noted round the right half of the anus, over a radius of about 3 cm. Voluntary and reflex con-

tractions of the anus and the bulbocavernous reflex were somewhat reduced. A mass was not palpable on rectal examination, and roentgenograms of the lumbosacral portion of the spinal column were negative. A caudal lesion was suspected. The patient was advised to go home, to follow palliative measures, and to return later.

He returned on April 6, 1925. The pain had persisted even more steadily than before, although it had been less intense; he had continued to arise at night, and he had learned that coughing, sneezing, riding in an automobile and bending down to put on his shoes influenced the pain adversely. At times he had had difficulty in expelling an enema. Control of urine had been normal.

On examination, the anus was patulous. Including it and completely around it for a distance of about 3 cm. the skin was completely anesthetic; a concentric

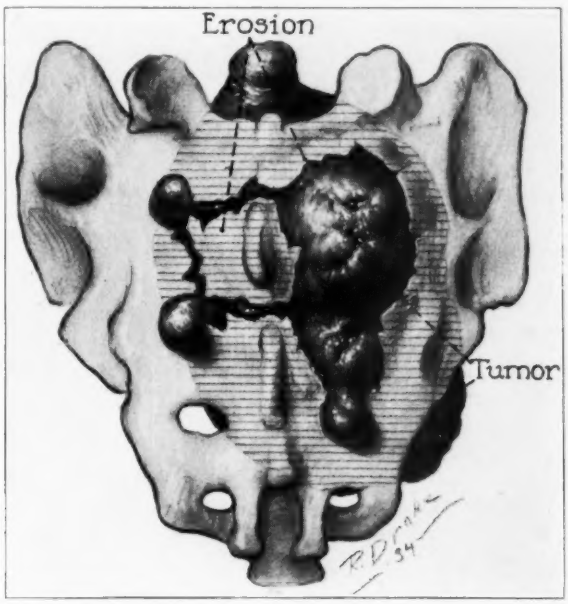


Fig. 5 (case 7).—Character of the tumor and destruction of bone by a sacral chordoma.

area of impaired appreciation of touch, pain and temperature extended about 4 cm. beyond the anesthetic zone. On rectal examination, a firm, smooth mass, the size of half an orange, lying in the median line below the promontory of the sacrum, was palpated. A roentgenogram of the sacrum disclosed a questionable shadow in this situation. The spinal fluid yielded a positive reaction for globulin but was otherwise normal.

On May 9, 1925, a tumor, 7 cm. in diameter, lying opposite the second, third and fourth sacral vertebrae, was partially removed. Roentgen therapy followed (fig. 5).

On Feb. 2, 1926, the patient reported that he had been more comfortable. Objectively the findings were unchanged save that roentgenograms of the sacrum now disclosed erosion of the bone.

On June 8, 1927, extensive destruction of the sacrum was noted in roentgenograms. A friable, cartilaginous tumor was removed (fig. 6).

On June 21, 1927, the patient was practically free from pain. Sensation around the anus was moderately impaired. The anal sphincter functioned normally. Chaddock's reflex was slightly positive on the left.

On June 9, 1928, the patient returned because of pain in the upper part of the right thigh. The right achilles tendon reflex was moderately reduced.

On July 30 the pain extended down the leg to include the right calf. The rectal sphincter was somewhat relaxed, the function of the bladder slightly impaired, and the right achilles tendon reflex was absent. Perianal sensation was markedly impaired throughout a radius of about 8 cm.

Fig. 6 (case 7).—Erosion of the sacrum by chordoma, anteroposterior view.

The patient returned on Jan. 4, 1929, because of marked swelling and weakness of the right leg. The leg had become weak gradually since the preceding August. In November the swelling had appeared. There had been pain in the right lumbar, sacral and testicular regions. For six months there had been some urinary retention and fecal incontinence. Power of erection had been preserved. The patient limped on the right leg, owing no doubt to the marked weakness of the right calf. The right achilles tendon reflex was absent; the left, markedly reduced. There was moderate impairment of superficial sensibility round the left side of the anus. The right leg, the scrotum and the penis were markedly edematous.

An operation on January 16 disclosed that the sacrum and right ilium were extensively involved by a tumor. On the following day the edema had disappeared.

The patient died on July 20, five years after the onset of his symptoms.

Microscopic examination of this tumor revealed a typical chordoma with several additional points of histologic interest. Many unusually good examples of physaliphorous cells were present, and also nonvacuolated cells, the vesicular nuclei of which were rounded and usually excentrically placed and contained a deeply stained, prominent nucleolus. These cells bore a striking resemblance to ganglion cells, but when they were stained with toluidine blue no Nissl granules were seen in their cytoplasm. These same cells, when stained for axis-cylinders by the silver impregnation method, did not have an affinity for silver; they had no processes, and axis-cylinders were not seen originating from any of them. Nuclear vacuoles were observed in many of the tumor cells, forming actual physaliphorous nuclei. These nuclear vacuoles did not give a positive reaction for mucus. A few of the cells were multinucleated, but mitotic figures were not found. The intercellular mucus was not a prominent feature. Tumor thrombi were present in a few of the thin-walled vessels which lay in the connective tissue stroma.

Case 8.—On Jan. 26, 1925, a man, aged 58, who was engaged in secretarial work, registered at the Mayo Clinic because of pain in the coccygeal region. This pain had appeared six months before and had been noticed first while the patient was sitting in a theater. Tenderness had been especially marked.

On rectal examination, a firm, insensitive, sacral tumor was palpated. A neurologic examination was not made; however, it was noted that the patellar and achilles tendon reflexes were present and equal. Roentgen examination of the sacrum gave negative results.

On January 30 the tumor, which had invaded the sacrum, was removed as completely as possible. Radiotherapy was then instituted. The man returned on April 25 and again on June 28, 1926, because of a persistent sinus. He had been free from pain since the operation. In December 1933, nine years after the removal of the tumor, he wrote that he felt entirely well.

Microscopic examination of the tumor showed the lobular structure of a chordoma. In the larger lobules the more centrally placed cells were arranged radially in narrow cords, widely separated by a colloid-like substance which gave a positive reaction for mucus. In the smaller lobules the cells were set close together, giving an epithelial appearance. Practically all the cells gave evidence of varying degrees of cytoplasmic vacuolation up to the huge physaliphorous cells. The content of some vacuoles also gave a positive reaction for mucus with the mucicarmine stain. Mitotic figures were not observed in any of the cells, and nuclear vacuoles also were lacking. The stroma of the tumor was scanty and was composed of fibrous connective tissue. A histologic study of this tumor showed that it was a typical chordoma and corresponded closely with the tumors previously described as such.

Case 9.—For eight months, a merchant, aged 61, had been suffering from increasingly severe, constant, aching pain in the region of the sacrum and right hip. During the same period a continuous sensation of tingling had spread over the buttocks. For three weeks he had been completely incontinent of urine and feces. For these complaints, the prostate gland had been treated; later, an abscess had been suspected. In September 1927 biopsy of a sacral mass had disclosed a chordoma. He was registered as a patient at the Mayo Clinic on Dec. 9, 1927.

The right lower extremity was moderately weak; the left, slightly weak. The achilles tendon and the external and internal anal reflexes were absent. There was hypesthesia for all qualities of sensation in the distribution of the first, second and third sacral nerves, with absolute anesthesia in the distribution of the fourth and fifth sacral nerves. Vibratory sensation was markedly impaired over

the malleoli. On rectal examination a sacral tumor was palpated; the right buttock also was infiltrated. Roentgenograms disclosed destruction of the sacrum and left ilium. A biopsy was made. Because of the extent of the tumor its removal was not attempted. Treatment with roentgen rays or radium was advised.

Microscopic examination disclosed that the tumor was composed of cellular lobules separated by narrow bands of dense, fibrous connective tissue. The cells at the periphery of the lobules were small and spider-like, and their processes formed a network of fine fibrils. The cytoplasm of the cells was scanty, and intracellular vacuoles were present in a few of them. Nuclear vacuoles were not observed. Mitotic figures were noted, but only occasionally.

Toward the centers of the lobules the cells were fewer, and their outlines were indistinct. These cells were separated by a slightly basophilic intercellular substance. The nuclei were shrunken and pyknotic. Cytoplasmic vacuoles of large size, some of which contained a colloid-like substance, were observed in many of the cells. The central portions of the lobules were avascular, but at the periphery numerous thin-walled blood vessels were seen, with the processes of the tumor cells attached to their walls, forming vascular attachments.

The presence of intracellular and extracellular mucus was demonstrated in sections stained with mucicarmine.

Histologically this tumor had the appearance of an atypical chordoma. Physaliphorous cells were present in some portions, whereas in other portions a sarcomatous aspect predominated. This was produced by the branching, spider-like cells previously described. Some of the cells had attachments to the perivascular spaces and simulated the arrangement seen in astrocytomas and ependymomas. These cells, however, contained cytoplasmic vacuoles which gave a positive reaction for mucus, and the transition between them and typical physaliphorous cells could be followed through the various stages.

Case 10.—On Aug. 19, 1930, a realty salesman, aged 25, registered as a patient because of pain and tenderness in the coccygeal and anal regions. The pain had appeared one year previously and had been excruciatingly severe but had lasted only two or three hours at a time. At first it had come once in two months, but more recently eight times daily. It had been aggravated by coughing and sneezing, and at times had extended along the inner and upper aspect of the thigh. Since the onset the patient had been constipated, and for seven months he had been troubled by dysuria. Removal of the coccyx in November 1929 had not relieved the pain. Examination of the spinal fluid elsewhere had disclosed an increase in globulin.

On rectal examination, a presacral tumor, from 3 to 4 inches (7.6 to 10.16 cm.) in diameter, was palpated. Roentgenograms disclosed sacralization of the fifth lumbar vertebra but otherwise gave negative results.

The patient left the clinic to be operated on elsewhere. The operation was followed by application of radium. Satisfactory relief was obtained.

On Jan. 7, 1932, he returned to the clinic. For two months he had suffered from attacks of aching, shooting pain in the sacrum and radiating to the perineum, right testis and inner aspect of the right thigh. For the same duration of time numbness had been present over the right buttock, and for three days catheterization had been necessary.

On examination, the anus was found relaxed, and on rectal examination, a sacral mass was palpated. An island, about 5 cm. in diameter, in which there was marked impairment of appreciation of touch, pain and temperature, was noted on the surface of the right buttock; surrounding the anus and confluent with the

area described, sensation of pin pricks was diminished; however, occasional stimuli gave great discomfort. Kernig's sign was moderately positive on the right. Roentgenograms disclosed cystic degeneration of the right side of the sacrum.

The tumor, 4 inches (10.16 cm.) in diameter and 2 inches (5 cm.) in thickness, was removed as completely as possible on Jan. 14, 1932. Neurologic examination on January 24 disclosed no changes in the findings. When the patient left the clinic he was free from pain, and function of the bladder had improved.

Microscopic examination of the tumor revealed that it had the structure and cellular characteristics of a typical chordoma. An unusually large amount of extracellular mucus was present in the central lobular zones, and many intracellular vacuoles containing mucus were present. Mitotic figures were not observed, and nuclear vacuolation was absent. Histologically, this tumor exhibited a high degree of differentiation.

COMMENT

In their general aspects these ten cases of sacrococcygeal chordoma resemble the seventy-five cases reported up to date. More males than females have had chordomas of the sacrococcygeal region. Machulko-Horbatzewitsch and Rochlin found twenty-six males and nine females who had sacrococcygeal chordomas; we found seven males and three females. Andler, as quoted by Machulko-Horbatzewitsch and Rochlin, attributed this to the greater incidence of trauma in males. The factor of trauma is intriguing. It may be worth noting that in two of our cases of sacrococcygeal chordoma in which there had been preceding injury the patients were women. In case 6 of this paper the patient had suffered a fall on the buttocks forty-six years before, and in case 4 a similar injury had taken place twelve years before. In some of the reported cases, as in that of Joyce,[10] the symptoms of the tumor dated from the time of injury.

Pain was present in all the cases, and in all but one it was the initial symptom. Tenderness was a common complaint. In four cases the pain in the sacrococcygeal region extended along the sciatic distribution. Subjective numbness was recorded as a symptom in seven cases and could be demonstrated in all the cases in which the patients had been subjected to neurologic examination, namely, six of the ten. Sphincteric disorders were present in eight of the ten cases.

In five cases, the physicians who had treated the patients earlier had had their attention focused on the presence of hemorrhoids. This is not only interesting, but suggestive. Further, the edema of the legs in two cases, while not an early symptom, and varicose veins of the legs in one, attest to a rather frequent interference with the local circulation.

The most valuable examination in these cases was digital exploration of the pelvis through the rectum. In nine cases a tumor could be pal-

10. Joyce, T. M.: Chordoma of Second and Third Cervical Vertebrae, S. Clin. North America **13**:85 (Feb.) 1933.

pated. Attention must again be called to the need of examining the hollow of the sacrum; too frequently the interest of the examiner leads him to limit palpation to the prostate gland, in which case a large sacral tumor may easily escape attention.

In four cases, roentgenograms gave evidence of destruction of the sacral vertebrae which, in appearance, suggested the presence of a malignant growth; in five the roentgenographic report was negative, as incidence of negative findings which, with recent improvement in roentgenologic technic, would probably not be so high now. No picture diagnostic of chordoma, as distinguished from other malignant tumors, could be established. Studies with iodized poppy-seed oil 40 per cent in the suspected cases of sacrococcygeal chordoma may produce diagnostic information before routine roentgenograms become positive.

The duration of the illness ran from eight months to eleven years, with one patient living in apparently good health nine years after the operation. In one case, in which the patient is still living, only a year has elapsed since the operation. Eight patients have died.

As in the cephalic cases, a preoperative diagnosis of chordoma apparently can be made only through biopsy, as was done in one case before the patient came to the Mayo Clinic. In only one case, encountered in 1926, was the possibility of "notochord tumor" entered on the records; this diagnosis was made by Dr. H. S. Plummer. The situation of the pain, which is usually lower than that observed with other caudal tumors, such as ependymal gliomas, the attending tenderness and the high and early incidence of perianal anesthesia and of sphincteric disorders are arresting phenomena. Coenen mentioned cold abscess, ileus and tumors of the sigmoid in differential diagnosis. This list might be increased without adding anything of material value.

Chordomas have been recognized as definite pathologic entities since Ribbert [11] demonstrated their origin from the notochord. Alézais and Peyron [12] and numerous other workers have made elaborate studies of their histogenesis and have considered notochordal tissue to be sui generis. From the embryologic standpoint, Williams [13] considered that notochordal tissue was distinct from all other tissues of mammals. The observa-

11. Ribbert, Hugo: Ueber die experimentelle Erzeugung einer Ecchondrosis physalifora, Verhandl. d. Kong. f. inn. Med. **13**:455, 1895; Geschwülstlehre für Aerzte und Studierende, Bonn, F. Cohen, 1904, p. 149. Ribbert, Hugo, and Steiner, Hermann: Ueber die Ecchondrosis physaliphora spheno-occipitalis, Centralbl. f. allg. Path. u. path. Anat. **5**:457 (June) 1894.

12. Alézais and Peyron, A.: Contribution à l'étude des chordomes. Chordome de la région occipitale, Bull. Assoc. franç. p. l'étude du cancer **7**:194 (March 16) 1914; Sur une tendance évolutive remarquable de certains chordomes. Passage de l'épithélioma au sarcome polymorphe, ibid. **7**:437 (July 20) 1914.

13. Williams, L. W.: The Later Development of the Notochord in Mammals, Am. J. Anat. **8**:251, 1908.

tions which have been made from study in ten cases of sacrococcygeal chordomas, showing a wide range of histologic variation, have led to the conclusion that notochordal tumors, although they may resemble either epithelial or mesodermal neoplasms, have specific characteristics by which they are distinguished. Briefly, these important characteristics are: (1) the formation of intracellular and extracellular mucus, (2) the presence of physaliphorous or huge vacuolated mucus-containing cells, (3) the lobular arrangement of the tumor cells, which usually grow in cords, (4) the occasional occurrence of vacuolation of the nuclei and (5) the close resemblance to notochordal tissue as seen in the nuclei pulposi of the intervertebral disks.

The production of mucus, which is the most primitive function of notochordal tissue, is also the most important characteristic of notochordal tumors. In the more malignant types of chordomas, in which the cells show various degrees of undifferentiation and mitotic figures are abundant, the ability to produce intracellular mucus remains to the last. This fact is well illustrated by case 3. In the highly differentiated types of chordomas the production of mucus is carried to an extreme; the cells tend to destroy themselves by overproduction. The histologic criteria on which a diagnosis of malignancy is based are the same as those applied to other neoplasms. The presence of mitotic figures and other evidences of activity, such as cellular pleomorphism, hyperchromatic and irregular nuclei and multinucleated tumor giant cells, have been observed by numerous authors and were found to be present in several cases in this series. As a rule, chordomas are well differentiated tumors and therefore of low malignancy. However, in contrast to their relatively benign histologic appearance, most of them possess markedly invasive and destructive properties; they invade even the lumens of the blood vessels, and this invading tissue was seen as tumor thrombi in case 7. Stewart [4] has compared these tumors to rodent ulcers.

Stewart [4] was the first to describe nuclear vacuoles in the tumor cells. He noted that they did not contain mucus or any substance which could be stained specifically. Since then nuclear vacuoles have been observed frequently, but their contents remain undetermined. Nuclear vacuoles were present in three of the ten cases reported here.

Certain cytoplasmic vacuoles do not react specifically to the stain for mucus, and these may possibly contain glycogen, as was claimed by Micotti,[14] Capell,[15] Nebelthau [16] and others. However, Kernohan, Wolt-

14. Micotti, Rinaldo: Sul cordoma del sacro, Policlinico (sez. chir.) **29**:265 (May) 1922.

15. Capell, D. F.: Chordoma of the Vertebral Column with Three New Cases, J. Path. & Bact. **31**:797, 1928.

16. Nebelthau, L. A., quoted by Coenen.[5]

man and Adson,[17] in their study of craniocervical chordomas, found that many vacuoles in these tumors give a scarlet reaction with Best's carmine stain for glycogen even after the tissue has been fixed for prolonged periods in solution of formaldehyde, U. S. P., which ordinarily precludes the demonstration of glycogen, since glycogen is highly soluble in fixatives containing water. These authors expressed the belief that the substance is not glycogen, but some allied substance, giving a nonspecific reaction. Similar results were obtained in the ten cases of this series, even after the tissue had been fixed for twenty-three years in a 10 per cent solution of formaldehyde, U. S. P.

Surgical Aspects.—Complete surgical removal of most sacral chordomas is practically impossible, since it would require removal of the entire sacrum to eradicate the disease. However, much can be accomplished in alleviating pain, retarding the growth of the tumor and controlling the neurologic symptoms by operative measures and radiotherapy.

It is apparent that activity of growth varies considerably, since one patient lived only two months following operation and two have lived more than nine years. The others lived, on an average, three and a half years. The treatment of all was about the same, namely, as complete surgical removal as possible, followed by roentgen therapy. In one instance only biopsy was performed before administration of the roentgen therapy.

Since the tumor originates from the notochord, in the sacrum and coccyx, a search must be made for a tumor that originates in the median line of both, which usually grows in all directions, producing destruction of bone by pressure and invasion. Frequently the tumor has destroyed the dorsum of the sacrum in a way in which it would be destroyed if it were possible for an explosion to take place from within. The tumor has eroded through the bone in places; sharp plates of bone have been lifted to unusual angles in other regions; soft boggy masses or nodules have been found protruding through the foramina, extending from the dorsal or ventral surfaces of the sacrum and coccyx. As the tumor grows it extends upward into the lumbar canal laterally into the ischia, and anteriorly into the pelvis. Hence, it is apparent that its growth is attended by severe local and radiating pains and dysfunction of the lower lumbar and sacral nerves. Operative measures are therefore employed with the hope of relieving pain and retarding the growth of the tumor.

The dorsal, median line approach, unroofing the tumor and effecting intrasacrococcygeal removal, appears to give the best access to the tumor with the least surgical shock. The ramifications of the tumor are readily

17. Adson, A. W.; Kernohan, J. W., and Woltman, H. W.: Cranial and Cervical Chordomas: A Clinical and Histologic Study, Arch. Neurol. & Psychiat., this issue, p. 247.

followed and removed; gentle curettage of the bony pockets permits macroscopic removal of concealed masses. Extrasacrococcygeal extension may require additional incisions. At all times, the utmost care must be employed to avoid injury to the sacral nerves, which may be seen running through the tumor. Bleeding is controlled by hot sponges and gauze packs.

Irradiation of the extremely vascular tumor undoubtedly retards invasion by the tumor but offers very little relief if the tumor is cartilaginous.

Surgical resection of the tumor, decompression of the sacrum and high voltage roentgen therapy do relieve pain, retard the growth of the tumor and prolong the life of the patient.

DISCUSSION

Dr. John L. Eckel, Buffalo: In 1924 I reported a case of chordoma which originated from the spheno-occipital region and which proved to be malignant. The patient was a man of 49. According to the history the first symptoms began two and one-half years prior to his admission to the hospital with pain in the cervical region and difficulty in moving the head. Eighteen months later tingling appeared in the fingers and shooting pains in the arms. The pains and tingling gradually increased until numbness of all of the extremities was present, and at the time of admission to the hospital the patient was quadriplegic and had to be catheterized. The muscles of the upper and lower extremities were definitely atrophied, and bulbar symptoms were apparent.

All of the laboratory tests of the blood, urine and spinal fluid gave negative results. Roentgenograms showed a dark shadow at the base of the brain, extending down the spinal canal to the cephalic surface of the second cervical vertebra.

Owing to the serious condition of the patient he was not operated on. He died in one month. At autopsy a tumor was noted which had arisen from the spheno-occipital region and had extended backward, compressing the cerebellum, the pons, the medulla and the left side of the upper portion of the spinal cord. It had not invaded the nerve tissue. The malignant tendencies of the tumor were shown by the actual invasion of the occipital bone and the upper two cervical vertebrae. Microscopically, the picture was much the same as that in the excellent slides shown by Dr. Fletcher.

Dr. Alfred W. Adson, Rochester, Minn.: There is nothing particularly diagnostic in the roentgenograms which would make it possible to distinguish a chordoma of the sacrum from any ependymal cell glioma. All of the ten patients who had sacrococcygeal growths were subjected to exploratory operations, all of which, however, I did not perform. I think the best approach is through the dorsal surface of the sacrum. Of the ten patients who were operated on, two are living. One has lived nine years and the other, one year; eight have died. The shortest period of life following operation was eight months, and the longest, eleven years. I am of the opinion that operation is indicated even though it is not curative, since it relieves local pain and retards lateral extension into the sacrum, as the tumor tends to grow in the line of least resistance. Roentgen therapy, I think, is of value in retarding growth. This is probably accomplished by destroying the smaller blood vessels.

GESTALT FUNCTION IN VISUAL MOTOR PATTERNS IN ORGANIC DISEASE OF THE BRAIN

INCLUDING DEMENTIA PARALYTICA, ALCOHOLIC PSYCHOSES, TRAUMATIC PSYCHOSES AND ACUTE CONFUSIONAL STATES

LAURETTA BENDER, M.D.
NEW YORK

A test for the visual motor *Gestalt* function, consisting of copying a group of *Gestalt* test forms, adapted from Wertheimer's [1] classic study of the *Gestalt* school of psychology, has been used in a wide range of organic and functional nervous and mental disorders. The *Gestalt* function may be defined as the function of the integrated organism whereby it responds to a given constellation of stimuli as a whole—the response itself being a constellation, pattern or *Gestalt*. All integrative processes within the nervous system occur in constellations, patterns or *Gestalten*. Integration occurs not by summation, subtraction or association but by differentiation, or by increasing or decreasing the internal complexity of the pattern in its setting. It appears that an integrated organism never responds in any other way. The whole setting of the stimulus and the whole integrative state of the organism determine the pattern of the response. Starting with this thesis, one may use a given stimulating constellation in more or less similar settings and study the *Gestalt* function in various pathologic integrative conditions in different organic and functional nervous and mental disorders. Such has been the task. Any pattern in any sensory field might be used as a stimulus. Visual motor patterns have proved most satisfactory, because the visual field most readily adapts itself to experimental study and especially because the sick person can usually cooperate with the simple test of copying a few test forms.

It has already been shown that the *Gestalt* function which is demonstrated by this visual motor pattern of copied form attains various integrative levels in normal development by processes of maturation in the growing child [2] as a result of definitely determined functional prin-

---

From the Research Department of the Psychiatric Division of Bellevue Hospital.

1. Wertheimer, M.: Studies in the Theory of Gestalt, Psychol. Fortschr. **4**: 300, 1923.

2. (*a*) Bender, L.: Gestalt Function in Mental Defect, Proc. Am. A. Study of Feebleminded, 1933, vol. 58, p. 1; (*b*) Gestalt Principles in Sidewalk Drawings and Games of Children, Ped. Sem. & J. Genet. Psychol. **41**:192, 1932.

ciples characteristic of the different maturation levels. The earliest responses are motor impulses in the form of scribbling. The biologic characteristics of the visual field determine the patterns which arise in the form of vortical movement tending toward whirls, closed loops and circles on a background. These perceptive features tend to adapt themselves to the motor impulse of scribbling in clockwise and dextrad horizontal directions (in a right-handed person) and gradually to adapt themselves to the stimulating external world, such as the test figures, under these experimental conditions. There is an effort to express the whole figure by means of closed clockwise loops on a background in concentric relations or in horizontal dextrad series. These are the first principles of *Gestalt*. In the growing child new principles arise by motor imitation of dots, dashes or zigzags, in series or in masses, or by experimenting with fragmentation or inhibition of the closed loop and constructing new forms and relationships in this way. Crossed forms, oblique and slanting relationships, a straight line as the distance between two fixed points, actual distances, size and number are evidences of higher or more sophisticated maturation levels. The principles of *Gestalt* function are expressed in such functional terms as movement, direction, series, masses, tendencies to closures, perseveration and inhibition. These principles arise primarily from motor impulses, and the temporal features are as important as the spatial.

Schizophrenia [3] disturbs the *Gestalt* function so that dissociative processes are shown in the *Gestalt* productions with some features of reversions to more primitive responses, especially characterized by movement of part of the pattern within the whole, the pattern itself not being entirely destroyed.

Studies of the *Gestalt* function in organic disease of the brain with sensory aphasia [4] show a disturbance characterized by a deterioration in form, with simplification and perseveration of the unit symbol. The visual motor pattern which is experienced in the copying of visually perceived form is reduced to its simplest element, usually the enclosed loop, and distorted by perseverative tendencies. The pattern tends to become reintegrated as the aphasia subsides. Weisenburg [5] in his recent extensive and carefully controlled study of aphasia emphasized that aphasia is not a unitary disorder but represents different types of mental and language disintegration. This disturbance of the visual motor

3. Bender, L.: Principles of Gestalt in Copied Form in Mental Defective and Schizophrenic Persons, Arch. Neurol. & Psychiat. **27**:661 (March) 1932.

4. Bender, L.: Disturbance in Visuomotor Gestalt Function in Organic Brain Disease Associated with Sensory Aphasia, Arch. Neurol. & Psychiat. **30**:514 (Sept.) 1933.

5. Weisenburg, T. H.: A Study of Aphasia, Arch. Neurol. & Psychiat. **31**:1 (Jan.) 1934.

Gestalt is one type of disintegration in the *Gestalt* function which is associated with sensory aphasia.

In mental defect a retardation in maturation processes has been shown to occur,[6] but not usually in such a way as to produce the same results as are possible for a younger normal child of the same mental age. Motor control may be better in the older defective person; smaller, or energy-saving, figures are the rule; the primitive loop is more freely used with less motor play and experimentation. There is evidence of

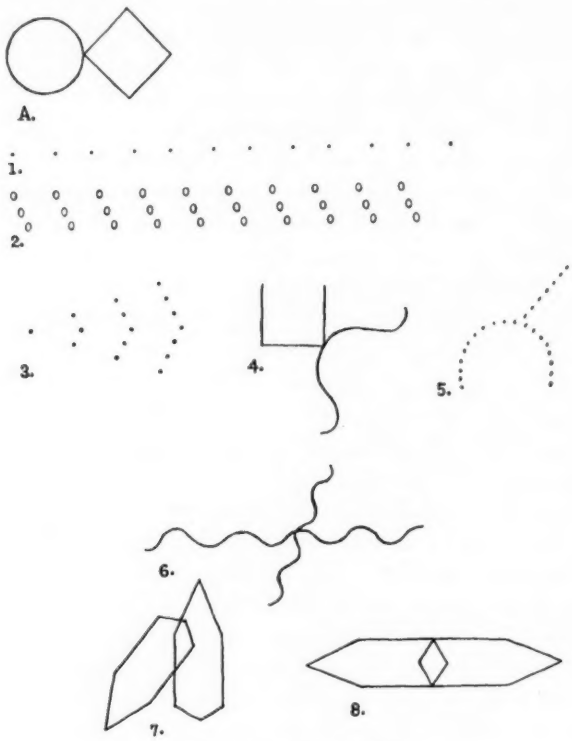


Chart 1.—Test forms.

different types of mental defectiveness. Fragmentation and dissociation may suggest a schizophrenia-like process, hyperkinetic features occur in connection with known encephalitic processes, and excessive perseveration of the primitive loop, which interferes with the integration of the pattern, suggests conditions similar to sensory aphasia.

It was the aim of the present study to investigate the disturbances in the functions of the visual motor *Gestalt* demonstrated by copying the visually perceived test figures, adapted from Wertheimer, in organic

6. Bender.[2a, 3]

diseases of the brain, including dementia paralytica, alcoholic psychoses, traumatic psychoses and acute confusional states.

It must be emphasized again that in copying these test figures (chart 1) the demonstrated *Gestalt* function includes both sensory and motor features, which do not lend themselves to an analytic separation without tending to destroy the produced *Gestalt* as readily as it would be destroyed if any perceived part of the pattern was separated from the whole. There are certain superficial motor features, such as the irregularities in the lines that occur in the immature child or in the tremulous polyneuritic person, and evidences of apraxia in aphasia and of ataxia in paralysis. But there are also more profound motor factors that arise from motor impulses which themselves are integrated into the *Gestalt* function. Thus, the child first displays a motor impulse to scribble, and gradually by experimentation there is a modification of the motor output toward imitation of the perceptive pattern. Other features which show energy-conserving qualities, such as the tendency to enclosed loops and to micrographia, as well as such features as perseveration and inhibition are undoubtedly related to the motor impulse. However, certain other features which may appear to be of motor origin are related to the perceptive features that are deeply embedded in the integrated organism, for example, the difficulties in slanting and oblique relationships, in straight lines and in square angles and crossed forms. These are all related to the primitive tendency to perceive form in loops. They are observed also in cutaneous sensibility.[7] These features are also seen in sensory aphasia in cases in which there is little apparent motor disturbance, and they are seen in defective persons who show other evidence of good motor integration. Of even greater significance, however, is evidence obtained by experimenting with adults with the tachistoscope, when the figures are experienced in the more primitive way. These results will be discussed more fully at another time.

DEMENTIA PARALYTICA

A recent intensive review of the various features in dementia in general has been made by Scheid;[8] this should be referred to for the literature. Kraepelin's[9] analysis of the symptomatology of dementia paralytica is in some way still classic. He emphasized that in the

7. Bender, L., and Schilder, P.: Streuung und Reihenverminderung im sensiblen Abbau, Deutsche Ztschr. f. Nervenh. **129**:146, 1933. Bromberg, W., and Schilder, P.: On Tactile Imagination and Tactile After-Effect, J. Nerv. & Ment. Dis. **76**:1 and 133, 1932.

8. Scheid, K. F.: Die Psychologie des erworbenen Schwachsinns, Ztschr. f. d. ges. Neurol. u. Psychiat. **67**:1, 1933.

9. Kraepelin, E.: General Paralysis, Monograph 14, New York, Nervous and Mental Disease Publishing Company, 1913.

domain of intellect one of the first changes is often a difficulty in perceiving and understanding outward impressions—"The patient is absent-minded, inattentive and does not grasp events transpiring about him with accustomed clearness." Kraepelin discussed the inability to fix the attention for a long period at a time, with more or less clouding of consciousness, disturbances in retention and memory and disturbances in orientation and time relations. His analysis of the paralytic disturbances in handwriting is well known. Schilder [10] has made a most intensive study in the psychology of dementia paralytica. Instead of the old concept of a defect he offered a new concept of a changed attitude and an insufficient technic in thinking. The process of thinking comes to a premature conclusion because attention is defective and unsuitable methods of thinking are used. Normally, the processes of thought include perception, the working over of the material and recollection. Schilder's experimental material was the repetition of a short story that was told to the patient. He was dealing with auditory perceptions, concepts and configurations, which are organized in time instead of the visual patterns of my material which are organized primarily in space. He emphasized that one is concerned with wholes and parts and their relationships. In the process of hearing the story the normal tendency is to anticipate the whole story with each sentence and thus organize it as a whole from the beginning. If this anticipatory adjustment fails, there remains only a word to word conception without regard for the sense of the whole. This anticipatory adjustment appears to me in some way to be a temporal *Gestalt* function. Schilder showed that as the story proceeds the adaptation requires that some anticipations be accepted and others rejected. In the patient with dementia paralytica there is a lack of interest in the whole relationship associated with the lack of anticipation. In perception the patient receives only whole impressions and does not adapt them to the newly added material and to his own life experiences, to his general affectivity and specific complexes as the normally integrated person does. Normally the working over of the material is merely a fuller understanding of the perception with further analysis and correction against experience, affectivity and the whole situation. The same occurs in recollection; there are always new combinations, selections and corrections. The patient with dementia paralytica does not correct sufficiently in this way—his critical power is diminished. He does not check against logic and experience. His general affectivity is weakened. His consciousness of the thing being right or wrong is weakened. Furthermore, an error once made is persistently followed. Perseveration occurs as

10. Schilder, P.: Studien zur Psychologie und Symtomatologie der progressiven Paralyse, Berlin, S. Karger, 1930.

a primitive feature. This is closely connected with a once accomplished configuration. The impulse to continue and conclude may be diminished, but at the same time there may be an increased impulse to productivity of a rhythmic motif by perseveration. Another feature is that the patient does not place the episode properly in its setting. The story is not considered as a historical event but as an experience of his own. The bringing together of individual parts into a whole does not occur, and if a total concept comes to completion it is not sufficiently structuralized. The outstanding characteristic of the content of the production of a patient with dementia paralytica is its banality or commonplaceness. While in the schizophrenic patient the disturbance occurs in the complex-determined material, in the patient with dementia paralytica it occurs somewhat more in the periphery of the psychic life, although not so far in the periphery as in aphasia and apraxia. In the patient with dementia paralytica the disturbance takes place in the superficial layers of fairly well developed concepts; the utilization of the concept is changed; there is a failure in the working over of the material, in the combining, correcting and checking of it, and there is a weakness in the consciousness of what is correct. There is a disturbance in the differentiation and integration of the parts of the psychic experience.

In discussing the question of *Gestalt,* Schilder took issue with the Koehler-Kofka-Wertheimer school, which claimed that the *Gestalten* are determined at the perceptive level. Schilder claimed that there is a constant remodeling, a production momentum—not only a *Gestalt* but a *Gestaltung.* He maintained further that the *Gestalten* at all levels are influenced by attitudes and experiences and by the general affectivity and the specific complex. He claimed that it is the active remodeling or combinations in *Gestalten* that are affected in dementia paralytica, while in aphasia and agnosia both the passive reception of the configurations (*Gestalten*) and the reconstruction (*Gestaltung*) are affected.

A general summing of Schilder's analysis may be expressed in these terms: The patient with dementia paralytica is not interested in the structure of things, in the nature of the parts, in their relation to the whole or in the relation of the whole to the context; furthermore, he shows a defective power in any active structuralization tending to lead to productions resulting from the adaptation of his receptive experiences to the world of reality. The developing child has certain impulses in the motor sphere and certain vortical characteristics of the perceptive fields. His problem is to produce symbols from these two functions which represent the external world. The demented person has lost the urge to make these adaptations, the power to perform the processes of correcting and selecting and the consciousness of his own error. He has also, as a resurgence symptom, the primitive motor impulse to perseveration of his own poorly consummated configuration.

Case 1.—A colored woman, aged 30, was transferred to the psychiatric division of Bellevue Hospital on Aug. 6, 1931, from the City Hospital; a diagnosis of dementia paralytica was made. She had been at the City Hospital since December in a semicomatose condition; the Wassermann reaction of the blood was 4 plus, and the serologic condition of the spinal fluid was typical of dementia paralytica; routine antisyphilitic treatment had been administered. On admission she said "I was all dead about Christmas. It was nice there, but I just got sick and tired of it. It seems now and then my mind goes away. I was dead three times, you know. I forget the name of the hospital."

The pupils were fixed to light; speech was defective to test phrases and was slurred. The patient was childish, emotionally unstable and confused. Memory was defective, and she was entirely disoriented. Speech was incoherent, disconnected and fragmented.

Gestalt Forms.—The patient's productions in chart 2 (see chart 9 for normal productions) show tendencies to make the figures very small and to fragment and

Chart 2.—Dementia paralytica. Note the micrographia, fragmentation and separation of the parts.

separate parts. The tendency to draw figures very small or to write small—micrographia—has been described by Gerstmann and Schilder,[11] who claimed that it occurs as a result of a weakening or poverty of the impulses. It is found associated with various diseases of the brain, such as encephalitis and sensory aphasia, and in the latter may occur only in the hand innervated by the hemisphere which contains the lesion. This patient not only produced small figures, but sketchy ones. Separation of parts of the figure tends to emphasize the primary members of the *Gestalt,* as in figures A and 4. Fragmentation, however, further divides the figure, usually in places not recognized by the *Gestalt* principles; thus squares, which are genetically simple closed figures, are fragmented into sides, and the crossed wavy lines are fragmented into four wavy lines and further fragmented into segments of the waves.

11. Gerstmann, J., and Schilder, P.: Zur Frage der Mikrographie, Ztschr. f. d. ges. Neurol. u. Psychiat. **67**:59, 1921; Mikrographie bei Sensorisch-Aphasischen, Arch. f. Psychiat. **74**:150, 1925.

In this case, then, a patient with dementia paralytica, with prolonged comatose periods and episodes of confusion with no real interest in the situation, showed in visual motor *Gestalt* responses a poverty of impulses, a tendency to fragment the structure of the *Gestalten* at points not always in keeping with genetic principles, but determined by the superficial appearance.

In an intellectual person incipient dementia paralytica shows rather typical features in the production of these visual motor *Gestalten,* which may be characterized by a certain stilted, excessively careful perfection that tends to be formalistic and to lack any personal interest, while at the same time there are nearly always some evidences of reversions to some primitive tendencies.

CASE 2.—A man, who appeared to be about 40 but who could not recollect his correct age, claiming he was 24 or 26 years old, had had one year of college educa-

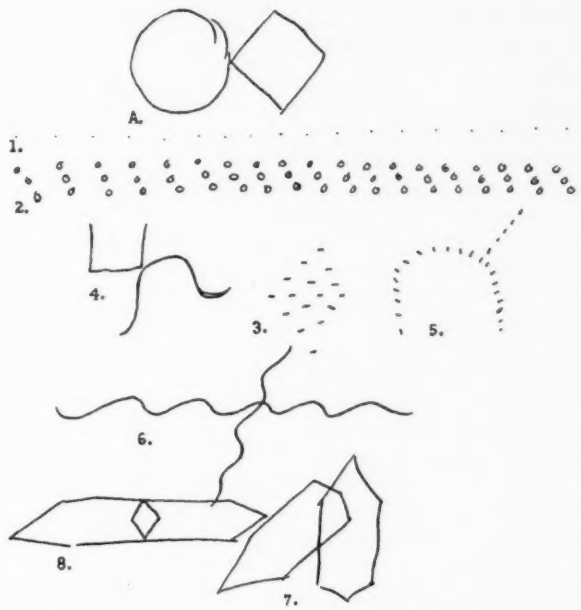


Chart 3.—Dementia paralytica. Note the formalistic perfection, perseverative tendencies and the substitution of dashes for dots.

tion and had been an actor. He was brought to the hospital as a prisoner on a charge of disorderly conduct because of resisting an officer who attempted to make him "move on" from a box on the street where he had been sitting for a day and a night.

The Wassermann reactions of the blood and spinal fluid were four plus; there were 20 cells in the spinal fluid, and the colloidal gold curve was 0122332100. He said that he had had antisyphilitic treatment for one year. There were incomplete Argyll Robertson pupils and slurring speech. The patient was dull and lethargic and would lie on the bed all day; he took no interest in anything except that he showed occasional outbursts of irritation. He could not calculate or recall accurately. He said: "I was sleeping on a fire escape—a landing. I had a box to lay on. The fellow took it. I asked them for it, and he would not give it to me so I kicked it from under him, and I picked up a brick."

The patient carried a drinking glass wrapped in paper. About this he said: "I don't want to drink after people. Why, I might get a disease. I took the cure for eight months. I must have gotten the syphilis off a glass." He was told that he seemed sluggish. This made him irritable. He said: "So that makes me insufficient? It does not. I don't have to take this off of you people. I will get out of here tonight."

Gestalt Forms.—The patient's productions on chart 3 show excellent qualities (compare chart 9). Note especially the correctness in figures 7 and 8. The stilted formalistic features are exaggerated in figures 4 and 5, and as a result the configuration in figure 4 is destroyed; the difficulty, however, is not in making angulated forms, which is the problem in normal genesis, nor in the tendency to exaggerate a series of arc forms, which is another common difficulty. The use of some substituted form, such as, in this case, the dash for the dot, is a characteristic feature of dementia paralytica, which will be discussed in subsequent cases. Primitive tendencies are seen in the monotonous perseverations of figures 1 and 2 to the edge of the paper.

Comment.—Several cases of dementia paralytica in which treatment with malaria or with the radiothermy technic had been used in the New York Psychiatric Institute have been studied by this method. The majority have shown the features of the group just described, namely, a formalistic, impersonal perfection with one or another feature suggesting either some form of reversion to primitive responses or some feature more or less typical of dementia paralytica. It should be said that most of the patients treated had possibly been selected for treatment because they were in the early stages of the disease and were originally of adequate intelligence; consequently they show the features of this group. It should also be said that they were all patients who had returned to the hospital because they had in some way failed to adjust in spite of the treatment.

In cases of productive dementia paralytica one finds a number of new features. One such case had already been discussed briefly from the point of view of differential diagnosis from mental defectiveness.[12] One of the most conspicuous features was the substitution of various letters or numbers for the dots in the dotted figures. Thus, figure 1, instead of being a series of dots, was the series of the alphabet from A to K. Figure 2 was then made as three horizontal series of M's and N's and finally McC's, the patient's own initials. Figure 5 was made of 8's; figure 4 was made like a single large 4, while the patient said, "That is not a four, I guess." In addition to figure 4, others were also constructed with wrong configurational principles, for example, figure 5, and figure 8 was made with the ends expanded instead of pointed. I may summarize by saying: The structure of the *Gestalten* is partially ignored (1) by disorienting them from their background, (2) by constructing them by principles suggested by their superficial appearance rather than their genesis and (3) by substituting some other figure for individual parts. The patient's own initial may be used, or some other familiar but inappropriate series may be substituted for the one offered.

Similar features are shown in the following cases:

CASE 3.—A colored man, aged 53, who had been a chef on railroads and steamships, said: "Next week I am going to go on a world tour with the millionaire Vanderbilts. I have worked for Governor Smith and President Roosevelt. I am the best cook in the United States. Everybody likes me. I have twenty-five shares in the Morgan line. Old man Morgan-Pierpont—I should

12. Bender, [2a] plate 9.

hope to tell you I do know him, etc." He was usually readily expansive in conversation and was always pleasant and amiable. He showed serious defects of memory. The Wassermann reactions of the blood and spinal fluid were four plus. The spinal fluid contained: globulin, three plus, and cells, 60; the colloidal gold curve was 0112332100. The pupils were irregular and reacted inadequately to light.

Gestalt Forms.—The productions in chart 4 show some tendency to make the figures a little small. Figure 1 is a series of small loops. Figure 2 is a slight variation from this in that the loops are gradually modified into D's. When the examiner pointed to the test form and asked: "What does this look like?" the patient said "They look like D's." The question was put in such a way that it might as well have referred to the whole figure, but the patient's interest was apparently focused on his own interpretation. In the same way figure 3 was made

Chart 4.—Dementia paralytica. Note the expansive features combined with moderate micrographia and some reversions to primitive tendencies.

of dashes; when asked about the figure the patient said: "It looks like dashes." But from the mode of his response it appeared that in some way he knew they were not D's or dashes. It will also be noted that figure 3 is disoriented on its background and that the single dot (dash) is separated from the rest of the figure, as sometimes happens in the productions of small children and defectives.

Case 4.—An Englishman, an oiler, aged 64, who had been in the United States for twenty years, was brought to the hospital in November 1930 as a prisoner on a charge of vagrancy. He had small irregular pupils, which did not react to light. The knee jerks were diminished. The Wassermann reactions of the blood and spinal fluid were four plus; the colloidal gold curve was 5544321000. The patient was confused and amiable and presented Korsakoff features. Comprehension and memory were poor. He said: "Yes, of course, I know where I am, but I don't know if you do or not. I'm right here. You ought to know that."

Gestalt Forms.—The productions (chart 5) show an excellent perfection of the general configuration. Dots, however, are always converted into figures. Figure 5 is disoriented on its background; figure 6 is fragmented at the point of crossing.

CASE 5.—A white man, aged 30, had been treated with malaria in a private hospital the year before, but the disease had continued to progress. At home he was threatening and hit the baby, so that the wife was afraid of him. He was dull, incontinent and unable to care for his personal needs. Speech was totally disorganized, irrelevant, incoherent, paraphasic and dysarthric. He said: "I am all right. He gave me gas. I sleep with gas. Give me temps in the ear. Good doctor—Bellevue Hospital—I mean what a doctor give the good weight 135. My boy is—I mean my wife—but the boy—I mean my wife hit the boy—I mean my son—I love my son (cries)."

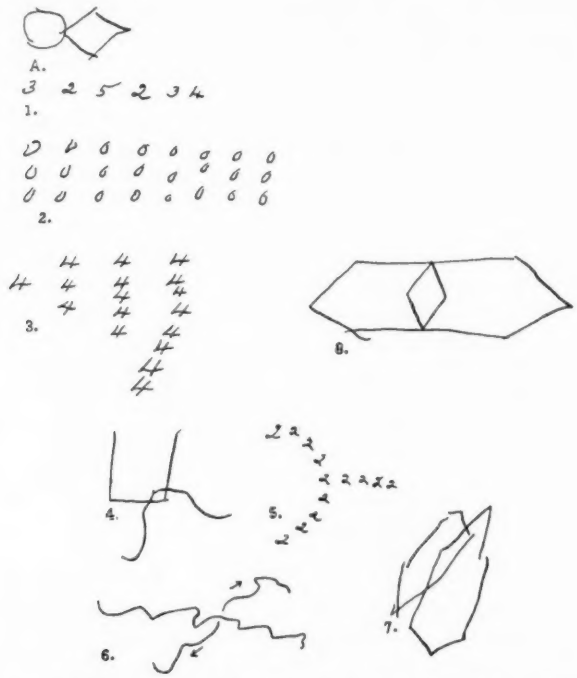


Chart 5.—Dementia paralytica. Note the expansive features.

Gestalt Forms.—The productions (chart 6) showed the primitive use of combinations of loops in figures A, 4, 6, 7 and 8, and in figures 1, 3 and 5, the use of dashes and numbers, characteristic of dementia paralytica. In figure 3 the patient has accurately represented the configuration in terms of numbers, counting each horizontal series of dots and offering the number in place of the form. Figure 5 may represent some similar effort. At the top is the patient's attempt to write his own name, John J—.

Summary.—When patients with dementia paralytica are asked to copy test figures various types of visual motor *Gestalt* responses are produced, depending in part on the type of clinical syndrome. It would

be of interest to correlate these responses with the localization of the lesions in the brain. The level of the original intellectual integration is probably also significant, as well as the personality as a whole and the situation. The higher intellectual levels are seen in the general contours and attempts at perfection in the productions. From time to time the patient's initial or other personal material is worked into the *Gestalten*. In the dull lethargic types, prone to comatose episodes,

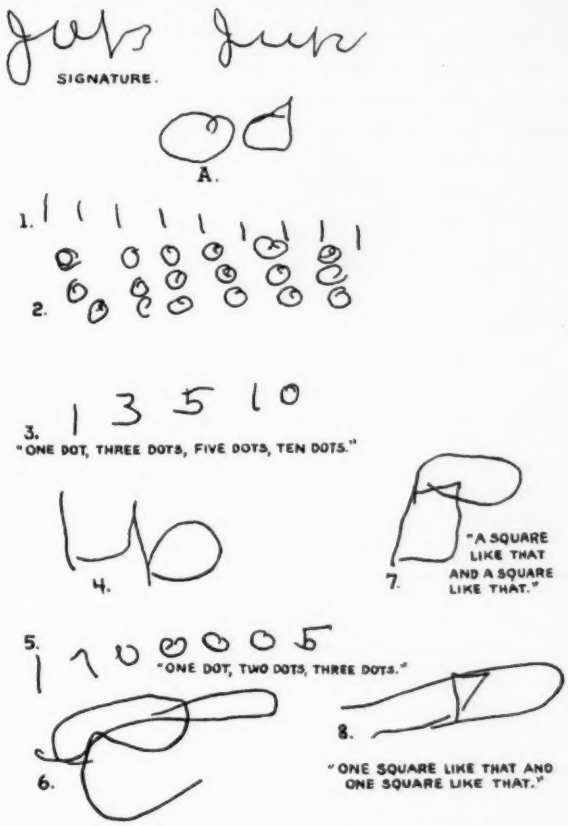


Chart 6.—Dementia paralytica. Note reversion to primitive tendencies with some expansive features.

the visual motor *Gestalten* show evidence of poverty of impulses and of fragmentation at artificial points in the configuration suggested by the superficial appearance rather than by the genetic *Gestalt* principles. It is possible that cases showing these features are those in which the lesion is more basal than cortical; this is suggested by the associated lethargic states and is compatible with the published reports of cases of epidemic encephalitis showing the same feature.[11] In the expansive types there is a tendency to substitute letters, numbers, dashes or the

patient's own initial for parts of the configuration, while the whole figure remains fairly intact. This may be akin to confabulation. The whole figure may be disoriented on its background. Later, it will be shown that this is a confusional feature. Parts of the form may be changed; thus, the two ends of figure 8 may be expanded, but nevertheless the whole figure remains nearly intact. The general principles of the *Gestalt* are preserved at all times. Some change of a minor nature happens to the concept after it is correctly conceived as a whole. One has the feeling that it is somewhat playful but rather senseless. Occasionally a form is copied in a way contrary to the *Gestalt* principle, while the patient remonstrates with himself and says, "It is not really that." Early cases of dementia paralytica in well integrated persons or cases in which treatment has been administered early show certain compensatory features. There is a tendency to formalistic but impersonal perfection. Nearly always, however, there is also some telltale feature suggesting one or another type of paralytic deviation, or reversions to some primitive feature such as the use of the closed loop or perseverations in horizontal dextrad directions. These primitive reversions are more common in cases with aphasic, agnostic or apraxic features.

ALCOHOLIC PSYCHOSES

There are a variety of mental disturbances caused by acute and chronic alcoholism, such as encephalopathia alcoholica with its typical organic lesions in the brain, which often progress to death, the Korsakoff syndrome, often associated with peripheral neuritis, acute and chronic delirium, acute and chronic hallucinatory states and acute confusional states, and various mixtures of these syndromes. In a psychologic, clinical and pathologic study of alcoholism Schilder and I [13] have differentiated the encephalopathic group from other types and have analyzed the symptomatology in relationship to the organic lesions in the brain. Clouding of consciousness is in the foreground of the psychologic syndrome, in which difficulties in perception play the most important part, associated with some delirious and confusional features, with difficulties in the integration of the perceived pictures. The picture is perceived incompletely and is not well integrated into the whole, or the whole is not well differentiated into its parts. With the clouding of consciousness are associated motor difficulties which are characteristic of this disturbance. They are rhythmic movements, especially of the arms and hands, associated with grasping, groping and pointing. Because of other features, such as poor attention and lack of cooperation, tremors and tensions in the arms and ocular disturbances, patients with encephalopathia alcoholica do not lend themselves well to this test.

13. Bender, L., and Schilder, P.: Encephalopathia Alcoholica, Arch. Neurol. & Psychiat. **29**:990 (May) 1933.

CASE 6.—In this atypical case of encephalopathia alcoholica, the patient died a few days after having attempted to draw figure A of the test group (chart 7). There are three efforts to draw the figure, each starting with the square and never attempting the circle, but becoming diverted each time by some perseverative behavior. The first time the patient continued the incompleted sides of the square into perseverated tails; the second time he made many perseverated strokes over the incompleted figure; the third time he completed the square but continued the last side into a dextrad stroke across the paper and then started to enclose the square in loops which are perseverated down the paper in simple strokes. In this case one sees the combined effect of the perceptive and motor disturbances typical

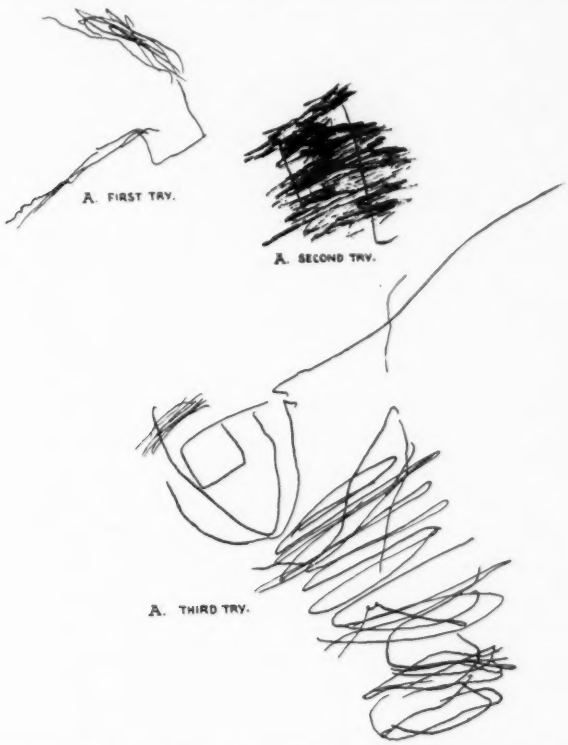


Chart 7.—Alcoholic encephalopathy. Note the incomplete figure with perseveration by rhythmic movements.

of this disease. The picture is never completed as a perceptive pattern, and finally the visual motor pattern is distorted by the motor impulse to rhythmic movement.

Comment.—The Korsakoff psychosis is differentiated from the encephalopathic state by the clearing of consciousness. The difficulties in the integration of the material is held to be more pronounced than the perceptive difficulties, and there are active tendencies to confabulation because of these integrative difficulties, especially of past material or memories. Bonhoeffer,[14] in an analysis of the mental

14. Bonhoeffer, K.: Die akuten Geisteskrankheiten der Gewohnheitstrinker, Jena, Gustav Fisher, 1901.

symptoms of the various types of alcoholic disturbances, recognized the perceptive difficulties and showed that they do not arise in the periphery or perceptive organ but are of central origin. On account of these disturbances and the slowing down of the mental processes there arise difficulties in the construction of an accurate picture of the outside world. That there are difficulties in the reception as well as in the working over and reproduction of material will be seen in case 7, which, however, in the beginning also showed some confusional and organic features.

Case 7.—A woman, aged 50, a college graduate and a school teacher, was admitted to the psychiatric division of Bellevue Hospital on June 9, 1932, with a clinical picture of alcoholic encephalopathy. She was emaciated and unable to walk,

Chart 8.—Reproduction of the test forms by a patient with alcoholic Korsakoff psychosis with features similar to alcoholic encephalopathy.

and lay helpless in bed; she was incontinent, tremulous, drowsy, confused and disoriented, with defective memory and confabulation. The pupillary responses to light were defective; speech was slurring; there was a general tremor; the tendon reflexes of the legs were hyperactive; the muscle bellies and nerve trunks were tender. There was a history of chronic alcoholism. The Wassermann reaction of the blood and spinal fluid was negative; the colloidal gold curve was 0011000000. On admission the patient could not cooperate with the test, but two weeks later, on June 21, she was improved and no longer toxic or tremulous; although she was still weak and the limbs were tender, the condition appeared more like a Korsakoff psychosis with peripheral neuritis. She was amiable, euphoric and talkative, confabulated and showed defective memory. The pupillary

reaction to light was present. She was cooperative with the test, anxious to do well; she made a great effort but was dissatisfied with the results.

Gestalt Forms.—The productions (chart 8), which were scattered over six sheets of paper, are reproduced only in part. The results are in many ways similar to those in case 6 (chart 7), a case of progressive encephalopathy. They show the same difficulty with individual parts of the whole figure and the same tendency to interrupt an incomplete figure by strokelike perseverations. These are not perseverations in form, but are perseverated motor impulses such as were described in the rhythmic movements in the encephalopathic cases.

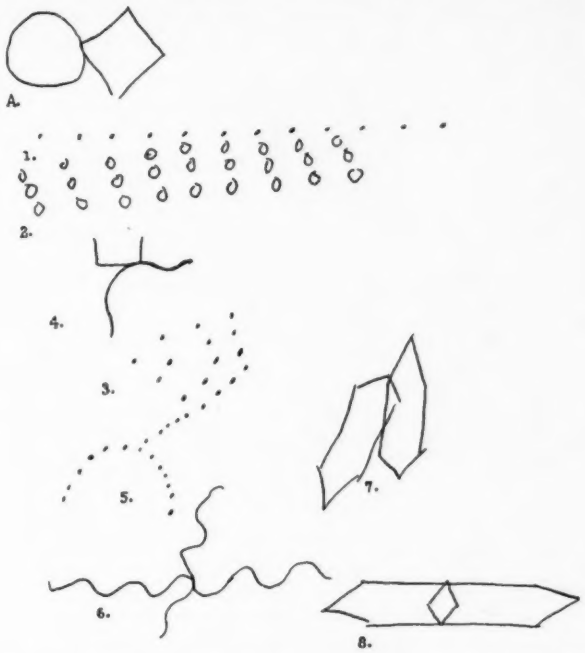


Chart 9.—Normal reproduction by the same patient as in chart 8 after recovery from Korsakoff psychosis (two weeks later).

They are often brought into play by making passive movements of the arms of the patients, which he will then continue rhythmically. This patient was herself baffled by her difficulties and attempted each figure many times, but invariably became distracted by some rhythmic process. From the results, however, it is clear that she was working with some concept, even though an incomplete one, of the test form in mind. In figure 2, for example, she started the figure with three distinct downward dashes, which are to be seen on the left side of the figure; she continued the motor pattern and soon distorted the figure and had difficulties in stopping. The continuation of the last stroke in figure 3 and of each extremity, especially the central dash of figure 5, is also seen.

Two weeks later the patient was much improved. She was able to walk and to care for her personal needs. She was clear and oriented. At this time she produced the test figures in an entirely normal manner (chart 9) and without any uncertainties. A couple of weeks later she was discharged from the hospital as recovered.

Comment.—A Korsakoff psychosis with less organic features and more confabulatory and confusional features is seen in the example given in my differential diagnosis from mental defect.[12] There are some tendencies to revert to primitive responses, to disorientation of the figure on its background and to changing dots into X's and 2's; these phenomena were seen in patients with an expansive type of dementia paralytica and appear to be a confabulatory feature.

Case 8.—A Scotchman, aged 49, was admitted to the hospital on July 11, 1932, in a state of alcoholic excitement—tremulous, agitated and disturbed—which passed into a hallucinosis. He did not recover in two weeks; on July 27 it was necessary to transfer him to a state hospital. The Wassermann reaction of the blood was negative. Apart from the tremulousness there was no organic feature. The

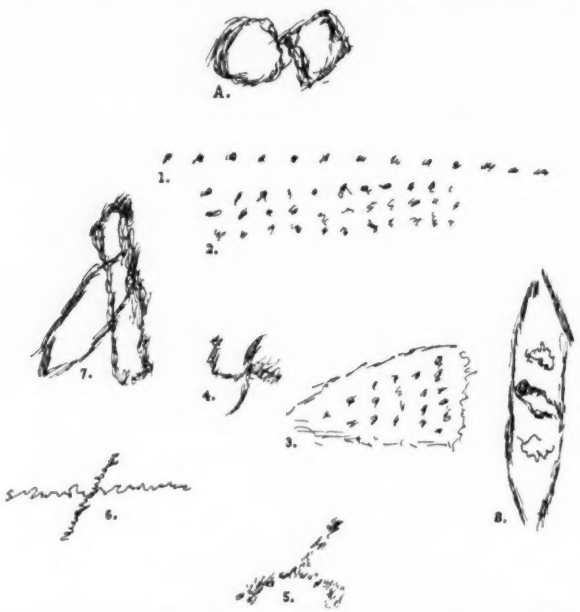


Chart 10.—Alcoholic hallucinosis. Note the perseverative tendencies in the outlines.

patient had vivid auditory and visual hallucinations of a distressing nature. He said: "Yes, I see my wife laid out there in her coffin. They shot her last night. I heard all about it over the radio. I was the one that put the spark in the air. They are going to kill me in front of her tonight. But we love each other too much." A week later, on July 18, he was no longer acutely toxic, but still had hallucinations and was subject to emotional episodes of fear and remorse.

Gestalt Forms.—The majority of the *Gestalten* are well perceived as a whole (chart 10). The patient has surrounded figure 4 with an outline to emphasize the whole contour and multiplied the internal figure in figure 8, as he said, "For good measure." The outstanding feature is the technic in forming the outline for the figures. There are some evidence of motor tremulousness and a tendency to go over and over each outline, which is undoubtedly similar to the tendency observed

in the other alcoholic psychoses with more profound organic involvement. It is possible that the outlines are also hazily perceived; nevertheless, the *Gestalt* as a whole is well perceived and reproduced. Three days later the figures (chart 11) showed a considerable improvement; as *Gestalten* they are well done, but there is the same tendency to repetitious movements in the outlines. There are no confusional features.

Chart 11.—Alcoholic hallucinosis. Reproduction by the same patient as in chart 10, three days later, with improvement.

Comment.—The alcoholic confusional states can perhaps be considered with the other acute confusional states. However, for the sake of comparison with other alcoholic conditions one example will be given here.

CASE 9.—A colored woman, aged about 45, had been a frequent visitor to the psychiatric division of Bellevue Hospital because of alcoholism. In each episode she appeared bewildered and confused. She usually recovered in from one to two weeks. At times she showed slight hallucinatory features, but not always. She

was admitted on Nov. 5, 1933, when she was acutely alcoholic, dull, confused and bewildered. On November 7 she attempted to copy the test figures.

Gestalt Forms.—The productions are seen in the upper part of chart 12. The patient did not attempt more than two of the figures. There are no motor tremors and few rhythmic processes. The lines are smooth. But there are difficulties of perception and difficulties in properly placing the figure on its background and in integrating the parts and their proper relationship to the whole. Figure 1, for example, is a mass of dots, which tends to be disoriented in the vertical direction until renewed effort gives a horizontal directional series of dots. Two further efforts, at five-day intervals (middle and lower part of chart 12), show better controlled series. Similar processes are seen at work in figure A.

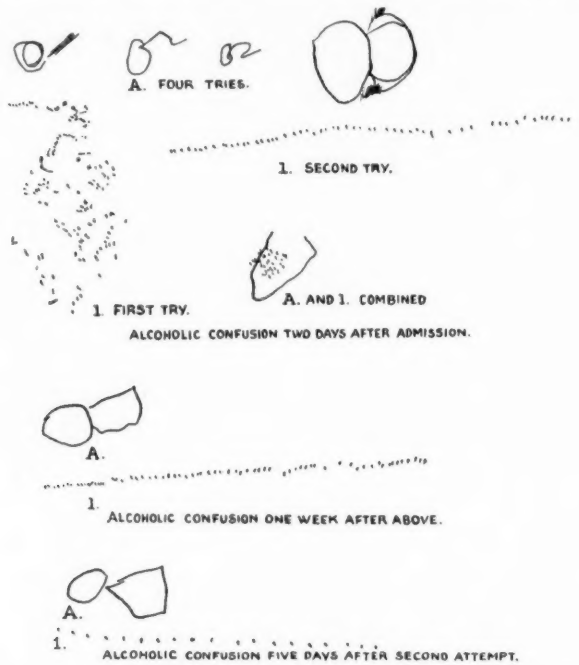


Chart 12.—Alcoholic confusion. Note the perceptive difficulties, the disorientation of the figure on its background and the disintegration of the figures.

Summary.—*Gestalt* disturbances in alcoholic psychoses are best approached with an understanding of the severe alcoholic encephalopathies, in which the progressive lesions about the ventricles of the brain may lead to death. This organic disturbance is associated with deep clouding of consciousness, with perceptive difficulties resulting in incompletely perceived *Gestalten* and motor difficulties with increased impulses to rhythmic movements. By this combination the visual motor *Gestalten* in copied figures are profoundly disturbed, so that the figure is reproduced incompletely and is distorted by perseverated strokes. In less

severe conditions there appear the Korsakoff psychosis, with less clouding of consciousness and more features of disturbed motor impulses in the perseverative tendencies of the figure produced. This is a perseveration of motor impulses or rhythmic movement and not a perseveration of form such as is seen in the sensory aphasias, although even in the latter the perseveration probably has a large motor element. In chronic alcoholic hallucinatory states the *Gestalt* as a whole is well perceived, but the outlines are hazy, perhaps partly from perceptive difficulties, partly from tremulousness and partly from the motor impulse to reiterate the line. In the confusional states there are less marked motor difficulties, but the perceptive difficulties are in the foreground and show disturbances in the integration of the parts into the whole and in the orientation of the figure on its background.

TRAUMATIC PSYCHOSES

Recently, Schilder [15] has analyzed the psychic disturbances after head injuries in patients in the psychiatric division of the Bellevue Hospital, many of whom were tested with this *Gestalt* test. Schilder discusses the analysis briefly and publishes illustrations. His analysis shows that following the initial state of loss of consciousness there is a stage of deep clouding of consciousness with disorientation in time and space, bewilderment, helplessness and retardation in perceptive functions, leading to difficulties in synthesis of the primitive impression into integrated wholes. "The *Gestalt* function is deeply impaired. In the visual motor *Gestalt* patterns, primitive structures appear. . . . It is probable that the clouding of the consciousness, the perceptive difficulties and the disturbances in the *Gestalt* function are partially independent from each other, but they are closely interrelated with each other and influence each other." He shows that the chronic Korsakoff picture may follow the acute posttraumatic confusional picture, which is distinguished from it by the absence of clouding of consciousness, and that in this posttraumatic Korsakoff state there may or may not be disturbances in perception and *Gestalt* function. The patient whose posttraumatic Korsakoff psychosis he describes in detail showed only minor disturbances in the *Gestalt* function in the way of more primitive responses. However, there are posttraumatic Korsakoff states which show rather severe disturbances in motor *Gestalt* responses. The difference in the reaction is possibly due in part to the localization of the lesion in the brain. In the more acute stages the whole brain is in some way involved. There is a general congestion and edema, with

15. Schilder, P.: Psychic Disturbances After Head Injuries, Am. J. Psychiat. **91**:155 (July) 1934.

bleeding in the subarachnoid space, and in cases which I have observed, universal perivascular hemorrhages, especially about the ventricular system, such as are found also in encephalopathia alcoholica. Russell [16] claimed that all parts of the brain suffer and that the site of the injury is of little significance in most cases. Bennett and Hunt [17] emphasized the multiple punctate intercerebral hemorrhages, cerebral edema and subarachnoid hemorrhages, which tend to lead to a diffuse cortical atrophy. Such pathologic changes appear to be associated with deep clouding of consciousness and disturbances in the synthesis of perceptive and *Gestalt* functions. More specifically localizable lesions may of course lead to more specific defects. Case 8 in my report on sensory aphasia [3] presented these features; there was a fracture of the skull, with gross injury to the left frontoparietal region, and a primitive type of reaction in the *Gestalt* function typical of sensory aphasia; the productions improved rapidly as the sensory aphasia improved after operative treatment.

Case 10.—A man, aged 42, who was admitted to the psychiatric division of Bellevue Hospital on Dec. 13, 1931, after having been injured in an automobile accident on December 5, had been found lying unconscious on the sidewalk. He had sustained an irregular fracture of the right side of the base of the skull and a depressed fracture of the left parietal bone. There was a left hemiparesis; the pupils were dilated and irresponsive, and there was nystagmus. The patient fell to the left when in the Romberg position. He was emotionally dull, but amiable, and there were Korsakoff features. Speech was slurred, but he was not aphasic. He said: "This is New Year's Eve. The accident was a month ago on Christmas Day."

Gestalt Forms.—The patient copied the *Gestalt* test on December 31 (chart 13), and produced some rather bizarre forms. In general the *Gestalt* principles are intact, though in a somewhat primitive form. There is serious distortion of the internal configuration of figures 4 and 6. There is no spatial disorientation typical of confusion. However, the individual parts of the configuration are distorted. Figure 1 is "some 2's all the way across," so that the figure becomes a dextrad horizontol series of connected 2's instead of dots. Figue 2 is a dextrad series of triads of jagged dots instead of loops. Similarly, figure 3 is a dextrad series of progressive lengths of crosses with a loop at the bottom. The other feature is the tendency to put loops or broad tails on nearly every figure. This shows some of the same features as the expansive type of dementia paralytica and the confabulatory type of alcoholic Korsakoff psychosis, with possibly some motor impulses to extra loops and tails.

Case 11.—The patient was transferred from another city hospital to the psychiatric division of Bellevue Hospital on Dec. 24, 1930, after having been hit on the head and knocked down while drinking, eight weeks previously. He was dull, confused and bewildered. He was not clear as to his environment and wandered about in a confused way. He confabulated constantly. Memory was defective for recent events, and he could not tell anything about the accident. He

16. Russell, R.: Cerebral Involvement in Head Injuries, Brain **55**:549, 1932.

17. Bennett, A. E., and Hunt, H. B.: Traumatic Encephalitis, Arch. Surg. **26**: 397 (March) 1933.

Chart 13.—Reproduction of the test forms by a patient with traumatic psychosis, showing Korsakoff features.

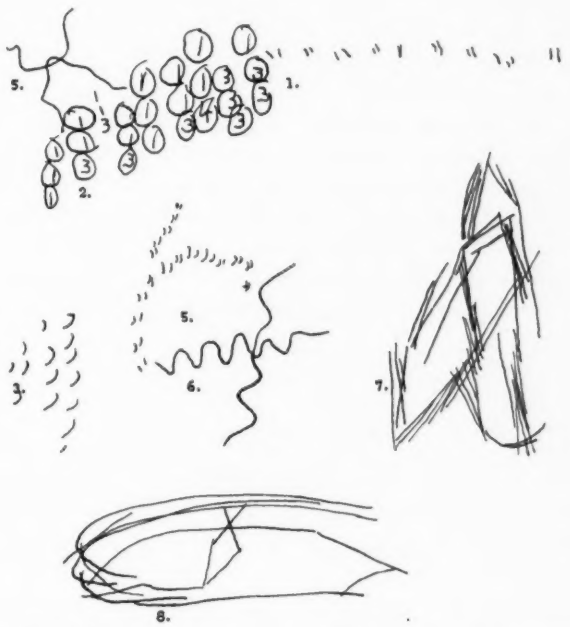


Chart 14.—Reproduction of the test forms by a patient with traumatic psychosis, showing Korsakoff features.

was retarded mentally and physically. He walked on a wide base and tended to veer to the right. There were flattening of the right side of the face, ptosis of the right eye, weakness in the right arm and slurring speech. Roentgen examination of the skull and examination of the spinal fluid gave negative results. He said: "I know where I am, but I forget the name of the hospital. I was down at the Post Graduate this morning (not true). I had an examination of my head. There is nothing the matter that I know of. The doctor came in and had a patient and asked me to give him a hand to bring him in. I brought him, and then he asked me to bring him to the Polyclinic Hospital. I did, and then he turned on the doctor. I interfered, and in the meantime I got hit in the mouth. A big crowd came into the clinic and into my home. I didn't know them; they were just noisy bodies."

Gestalt Forms.—The visual motor *Gestalt* productions (chart 14) show certain characteristics of the Korsakoff features such as were shown in cases of expansive dementia paralytica and alcoholic Korsakoff psychosis. The general *Gestalt* principles are intact, though the individual parts of the figure are modified or replaced, but not in such a way as to interfere with the configuration as a whole. Dots are duplicated in figures 3 and 5; the loops in figure 2 are filled in with numbers. The outlines in figures 7 and 8 are reiterated several times. Both motor and sensory impulses appear to play a part.

Summary.—The acute confusional stage following head trauma is characterized by clouding of consciousness with difficulties in the synthesis of the perception and *Gestalt* function. Visual motor *Gestalten* produced by the copying of figures show reversion to primitive features and confusional features, which are seen especially in the disorientation of the whole figure on its background. As the clouding of consciousness clears, and a chronic Korsakoff picture is left, there may or may not be disturbances in perception and *Gestalt* function. In some cases in which the injury is apparently severe and associated with signs of neurologic disturbances, Korsakoff features appear in the visual motor pattern. They are characterized by retention of the configuration as a whole and proper orientation of the figure on the background, but with a tendency toward some reversion to primitive responses and with modifications or substitutions in parts of the figure in such a way as not to interfere with the structure of the *Gestalt*. These features seem to be related to the confabulatory tendencies in speech and to pathologic motor impulses.

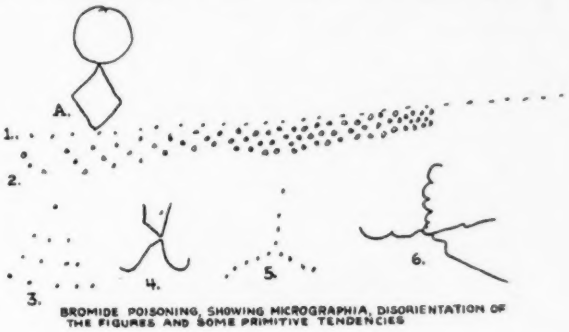
ACUTE CONFUSIONAL STATES

Acute confusional states occur in all forms of intoxication, whether endogenous or exogenous. They may also occur in connection with organic diseases of the brain and sometimes with schizophrenic or manic-depressive psychoses. Schilder [18] described the confusional states (or amentia) with perplexity as the central manifestation, in which

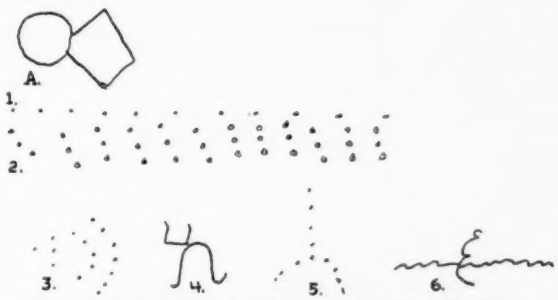
18. Schilder, P.: Introduction to Psychoanalytical Psychiatry, Monograph 50, New York, Nervous and Mental Disease Publishing Company, 1928.

"perplexity is the correlate of an inadequate comprehension of the environment with the additional symptom of dissatisfaction with the inadequacy."

Confusional features have already been shown in dementia paralytica (charts 4 and 5), in alcoholic confusional states (chart 10) and in posttraumatic confusional states,[15] with the following features: (1) some moderate degree of reversion to more primitive responses, (2) some difficulties in integrating parts of the figure into the whole *Gestalt,* (3) a nearly specific tendency of disorienting the whole figure



BROMIDE POISONING, SHOWING MICROGRAPHIA, DISORIENTATION OF THE FIGURES AND SOME PRIMITIVE TENDENCIES



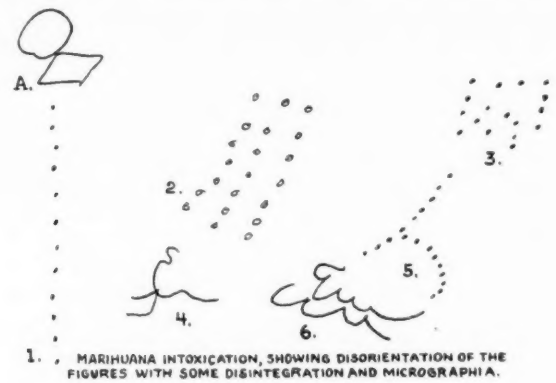
PARTIAL RECOVERY FROM BROMIDE INTOXICATION. (ONE WEEK AFTER ABOVE.)

Chart 15.—Reproduction of the test forms by a patient with an acute confusional state following bromide intoxication.

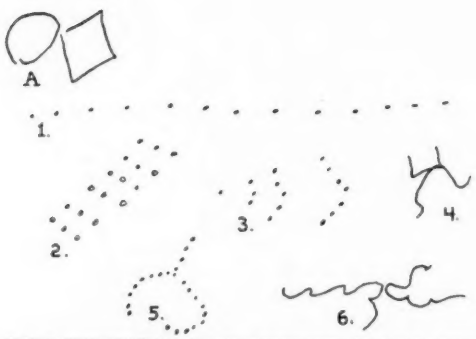
on its background. The last feature has appeared to be the most characteristic of the confusional state. The figure itself is complete but is upside down, in mirror reversion or turned around at an angle of 45 degrees. In the *Gestalt* theory, Kofka[19] has claimed that the first principle is the relationship of the figure to its background. The background may be looked on as a part of the *Gestalt* and this disturbance in orientation as a disturbance in the most fundamental principle in

19. Kofka, K.: The Growth of the Mind, New York, Harcourt, Brace and Company, 1928.

Gestalten. In other terms, the background is the environment, and this disturbance may be considered as an inadequate comprehension of the relation of the visual motor pattern to its environment. In still other terms, it may be considered as a disturbance in spatial orientation. This feature may also be seen in schizophrenia.[3] It may be demonstrated in any type of confusional disorder in organic or toxic states. I have observed it also in postoperative conditions, chorea minor, cardiac



MARIHUANA INTOXICATION, SHOWING DISORIENTATION OF THE FIGURES WITH SOME DISINTEGRATION AND MICROGRAPHIA.



PARTIAL RECOVERY FROM MARIHUANA INTOXICATION. (NINE DAYS AFTER ABOVE.)

Chart 16.—Reproduction of the test forms by a patient with an acute confusional state following marihuana intoxication.

conditions, bromide and marihuana intoxications and postepileptic confusional states. The following cases are selected examples of the last three conditions.

CASE 12.—A woman, aged 36, came to the hospital following the ingestion of an excessive amount of sodium, potassium and ammonium bromide in a fit of despondency over a runaway husband. She was lethargic, but somewhat agitated and emotionally unstable, and was constantly struggling against the urge to sleep. She was somewhat tremulous, and the tongue was coated. She appeared toxic. She seemed

bewildered and complained of feeling "mixed up in her head." Speech was slurring and tended to become incoherent as she talked of her troubles. She was clear as to the episode that led to her admission.

Gestalt Forms.—The patient performed the visual motor *Gestalt* test on the day of admission (upper part of chart 15). There is apparently some tendency to micrographia, which is in keeping with the drowsy state. Several figures are disoriented on their background, especially figures A and 3. There are primitive features in figures 1 and 2, in the tendency to make figure 1 a simple dextrad

Chart 17.—Acute confusional state, postepileptic confusion. Note the disorientation of the figures.

series, to make figure 2 a mass and to perseverate in both unnecessarily. Figure 3 also shows the primitive feature of arcs instead of angles. There are some difficulties in the integration of figure 4. A week later, the productions (lower part of plate 15) were much improved.

Case 13.—This case of marihuana intoxication has already been reported at length by Bromberg [20] among a series of cases, in several of which the visual motor *Gestalt* test had been performed. According to Bromberg, this condition shows among other symptoms "in the visual sphere a primitive level of perceptive integration." Case 8 in Bromberg's series is characterized by him "as an admixture

20. Bromberg, W.: Marihuana Intoxication, Am. J. Psychiat. **91**:303 (Sept.) 1934.

of toxic features due to marihuana with psychotic features of a functional type . . . a schizophrenia on symptomatic basis." The patient, a Negress, aged 31, had been smoking "reefers" and was admitted to the hospital because of peculiar behavior. She was dull, inattentive, apathetic, surly, suspicious and bewildered. She described the typical motile, colored visual hallucinations as well as hallucinations in other fields.

Gestalt Forms.—Two days after admission the patient copied the *Gestalt* figures as they are seen in the upper part of chart 16. Nearly all the figures are disoriented on their background; there is some tendency to micrographia, with some difficulties in the internal integration, as in the crossing in figure 6, and a consequent reversion to more primitive tendencies. Nine days later (lower part of chart 16) the visual motor responses were much improved, although minor difficulties still persisted, as in figure 2.

CASE 14.—A Negress, aged 42, was suffering from a postepileptoid confusional state in which she was dull, disoriented for time and place, bewildered and unable to get about the ward to care for her personal needs. She was also very irritable.

Gestalt Forms.—The productions (chart 17) show the same features of moderate micrographia, which are to be associated with the dulness, as are seen in connection with the lethargic types of dementia paralytica: disorientation of the figures on their background, as in figures 1, 2 and 6; difficulties in the integration of figures 3, 4 and 7 and secondary primitive reversions.

Summary.—The disturbance in acute confusional states resolves itself into a disturbance in the integration of the parts of the figure to the whole and of the whole to its background or situation. The primitive reversions are secondary to this primary difficulty. When micrographia occurs it is associated with the poverty of impulses observed in cases showing lethargy or dulness.

GENERAL SUMMARY

1. Visual motor experiments and tests consisting of the simple copying of selected figures from Wertheimer's series have proved of value in the study of the genesis and nature of the *Gestalt* function in visual motor behavior and of integrated mental disturbances in the visual motor field in various mental and nervous diseases.

It has already been shown that:

2. In normal children the visual motor *Gestalten* arise genetically from the integration of motor impulses and the biologic characteristics of the visual fields, and in development pass through definitely determined maturation stages.[21]

3. In organic disease of the brain associated with sensory aphasia the characteristic feature is the reversion to the primitive response with the simple closed loop, which is perseverated with resulting distortion of the integrative principle.[4]

4. In schizophrenia schizoid dissociative features may be demonstrated by this test.[3]

21. Bender (footnotes 2 and 3).

5. In mental defectiveness there are several different types of retardation in the maturation of the visual motor *Gestalten* dependent on determinable factors.[22]

6. In the present study of disturbances in the visual motor *Gestalten* in organic disease of the brain, the following conclusions have been reached:

A. In dementia paralytica there may be evidence of poverty of impulses, with micrographia, fragmentation and separation, especially in cases associated with lethargy or dulness. In the expansive types of dementia paralytica there is a tendency to substitute letters, numbers, figures or personal material, such as the patient's initials, for parts of the figure while the *Gestalt* as a whole appears intact. This may be akin to confabulation. There may be confusional features in which the figure is disoriented on its background. In nearly all cases the concept as a whole is preserved, but something of a secondary nature happens to the concept before reproduction. Fairly well compensated cases of dementia paralytica show productions that are formalistically but impersonally perfect, but these productions are almost invariably further marred by one or another telltale feature suggesting one of the features of dementia paralytica already mentioned or tendencies to primitive reversions.

B. In alcoholic psychoses the disturbances in the *Gestalt* function are best approached with an understanding of the severe alcoholic encephalopathies in which the progressive lesion in the brain may lead to death. This is associated with a deep clouding of consciousness, with perceptive difficulties resulting in incompletely perceived *Gestalten,* and in motor difficulties with increased impulses to rhythmic movements. By this combination the visual motor *Gestalten* in copied figures are profoundly disturbed, and the figure is reproduced incompletely and distorted by perseverated strokes. In Korsakoff psychosis, with less clouding of consciousness, the motor impulses to perseverative tendencies in the figure produced may be more prominent. In the chronic alcoholic hallucinatory states the *Gestalt* as a whole may be well preserved, but the outlines are hazy, perhaps partly from perceptive difficulties, partly from tremulousness and partly from the motor impulse to reiterate the lines. In the alcoholic confusional states there are less marked motor difficulties, but the perceptive difficulties are in the foreground and show disturbances of integration of the parts into the whole and in the orientation of the figure on its background.

C. In traumatic psychoses the acute confusional stages following the trauma are characterized by clouding of consciousness, with difficulties in the synthesis of the perception and the *Gestalt* function. Visual

22. Bender.[2a, 3]

motor *Gestalten* show reversions to primitive features. Especially there is seen the disorientation of the figure on its background. As the clouding of consciousness clears and a chronic Korsakoff picture is left, there may be typical Korsakoff features characterized by correct grasp of the figure as a whole and its orientation on its background with a tendency to some reversions to primitive responses and bizarre replacements of parts of the figure without interference with the structure of the *Gestalt*.

D. In acute confusional states the disturbance resolves itself into difficulties in the integration of the parts of the figure to the whole and of the whole figure to its background or situation. Tendencies to primitive reversions are secondary to this primary difficulty.

DISCUSSION

Dr. Max Wertheimer (by invitation): Dr. Bender's experiments are interesting; I hope that she will be able to continue this work, which involves many problems. It is not possible in so short a time to formulate the problems of the *Gestalt* theory. The investigations of Dr. Bender are of twofold interest: first, from the point of view of theory and second, from that of differential diagnosis. Concerning the second point, I wish to ask Dr. Bender whether she thinks that she would be able to make use of her results in differential diagnosis. Dr. Bender's findings generally are in agreement with the *Gestalt* laws, as far as I can see. The method which Dr. Bender has chosen for practical reasons, the method of drawing a thing by sight, of slowly copying a given drawing, which is continuously in view, is a somewhat dangerous method of solving the problem because it has, under certain circumstances, a slight tendency toward disintegrating figural patterns; it is also a complicated method, because it is not known in each case what is conditioned by the tendencies of the visual field and what by motor abilities and tendencies; the tendencies in both visual and motor patterns are mutually interwoven in the results. I agree that the two are closely connected, but the connection is not as simple as one may be tempted to infer. In Berlin and in Frankfort my co-workers and I tried to investigate and to use various methods specifically adapted to visual and to motor questions; in some cases the results were, up to a certain point, very different in effect, even though they agreed in principle.

Decided disturbances of figural patterns occur in cases of alexia, agraphia, aphasia, etc. In such cases there is often a great lability in the grasp of a figural pattern. The subject is incapable of conceiving and holding fixed, clear, integrated figural patterns; there is a tendency toward simpler, less integrated, less secure *Gestalt* processes.

It is interesting to note in the results of Dr. Bender how personality factors can be discerned in these drawings. Dr. Bender pointed out, for example, the tendency to fantastic embellishments in certain cases. The drawings sometimes show various traits of character; for example, some are painfully awkward and petty; some grotesque; some, cold and stiff; some, pompous. These and other tendencies often develop together with psychic illness and can be most clearly studied in the cases of sick painters. In some cases I have found a kind of interesting negativism. I believe that it is worth while to study these traits of character explicitly by experiment; *Gestalt* problems are also present here.

DR. DAVID M. LEVY: The application of *Gestalt* psychology to the field of visual perception will not, I think, interest most neurologists as much as its possibilities in the whole field of social behavior. First, however, I wish to point out a possible application of the *Gestalt* function in the field of visual perceptions to a test that is being used in psychiatric work. In the Rorschach test there is a series of ink blot pictures to each of which there is a strong tendency to respond in the first reply with a single concept. Since some of the pictures contain disparate and well separated blots there is greater difficulty in seeing them in that way. However, the patient is never asked to represent such a concept. There seems to be a natural striving to see the disparate elements as a conceptual unit. Beck, in studying that question, has shown that there is a distinct correlation between the number of so-called "whole responses" and the intelligence of the patient, with special reference to this tendency. Also there are differential responses to the test in which this fusion is lost. For example, a patient with melancholia hardly ever sees the pictures as wholes but is reduced to attacking only small elements of the pictures, showing that in this function of *Gestalt* an emotional element is required. Its absence or retardation reduces the patient to a lower level of concept formation; it affects the groping of *Gestalt*.

An application of *Gestalt* psychology to the general field is best illustrated, I think, in the principle of closure that Dr. Wertheimer referred to. The concept of a functional unit in the field of neurology is familiar in the reflex arc. Two or more neurons in functional relationship make up this unit. When the arc is reduced to its separate neurons the unit is fractured, and one can no longer talk in terms of physiologic function. The arc in terms of function is an irreducible unit. In the same way the social act may be regarded as a unit. Social acts, like the experiments in visual perception, must be closed, as in the attempt to fuse disparate elements in the Rorschach test into a concept. The application I am making of the act as a unit of behavior comes from the philosophy of Professor Meade. Consider, for example, the case of a savage who while fishing allows his pole to dip into the water and sees that the pole is bent. His behavior stops. He attempts to explain that act. His explanation is that some demons under the water are pulling the rod down. Why does he take the trouble to find an explanation? Why cannot he let behavior go on without interrupting his fishing? There is apparently something instinctive which requires closure, something like the following *Gestalt* experiment: Students are paid a certain amount to fill a barrel with water by using a cup at a time and before the barrel is quite full they are paid and told that the game is ended. Every one sneaks back and finishes filling the barrel.

In regard to the incomplete act there is an interesting application in the writings of Freud. It occurs only on one occasion, so far as I know, and that is in the explanation of a real neurosis. In that report a number of the symptoms are explained because of the "incompleteness" of the sexual act. It is from the physiologic incompletion that the psychic difficulties arise. One may wonder what possible changes might have occurred in the theory if this idea of incompleteness had been stressed instead of the idea of conflict as a battle of opposing forces, so basic to the theory of psychoanalysis. It is in the direction of the act as a unit of behavior that I see the application of *Gestalt* to social psychology.

CALCIUM CONTENT OF THE CEREBROSPINAL FLUID, BLOOD SERUM AND SERUM ULTRAFILTRATE

ITS RELATION TO THE CLINICAL FINDINGS IN EIGHTY NEUROPSYCHIATRIC PATIENTS

JOSEPH J. MICHAELS, M.D.
BOSTON
AND
OLIVE M. SEARLE, PH.D.
ANN ARBOR, MICH.

According to Elwyn,[1] fundamental metabolism, which is concerned with the inorganic salts in relation to the vegetative nervous system, is controlled by a center in the hypothalamic region. Schilder [2] expressed the belief that this region is significantly related to the affective layer of the personality. The increase of neuromuscular irritability in calcium deficiency has long been known (Loeb [3] and Mathews [4]). Kraus and Zondek [5] stated that the effect of an increase in calcium is analogous to that of the action of the sympathetic, and the effect of increased potassium to that of the vagus, system. It would seem much more simple to demonstrate the effects of variations in the calcium content at lower levels of psychobiologic activity, e. g., in a nerve-muscle preparation, with a minimum of variables, than at the higher levels of the personality, e. g., in impulsive, uninhibited behavior, in which the variables may be legion. A review of the literature on blood calcium as it pertains to neuropsychiatric considerations shows many conflicting reports; on the one hand, almost startling results have been reported; on the other, there is lack of confirmation by reliable workers.

From the Boston Psychopathic Hospital and the State Psychopathic Hospital, Ann Arbor.

1. Elwyn, Herman: Edema, Am. J. M. Sc. **180**:781 (Dec.) 1930.

2. Schilder, Paul: Brain and Personality, Washington, D. C., Nervous and Mental Disease Publishing Company, 1931.

3. Loeb, Jacques: On an Apparently New Form of Muscular Irritability (Contact Irritability?) Produced by Solutions of Salts (Preferably Sodium Salts) Whose Anions Are Liable to Form Insoluble Calcium Compounds, Am. J. Physiol. **5**:362 (July) 1901.

4. Mathews, A. P.: The Nature of Chemical and Electrical Stimulation: I. The Physiological Action of an Ion Depends upon Its Electrical State and Its Electrical Stability, Am.J.Physiol. **2**:455, 1904.

5. Kraus, F., and Zondek, S. G.: Ueber Die Durchtränkungsspannung (Mit besonderer Rücksicht auf die Bedeutung der Electrolyte), Klin.Wchnschr. **1**:1773 (Sept. 2) 1922.

Henry and Ebeling,[6] Armstrong and Hood,[7] Jacobi [8] and Scholberg and Goodall [9] found that the serum calcium in patients with psychoses was within normal limits. Tómasson [10] and Klemperer [11] reported higher values for serum calcium with increasing excitement and lower values in association with the depressive states. In Gullotta's [12] study of thirty-two patients with dementia praecox, 47 per cent showed an increase in the serum calcium and 18 per cent a diminution. The stage of catatonia was accompanied by a decrease of the calcium content of the blood and the state of excitement by an increase. Futer and Weiland [13] examined one hundred and eight patients with various neuropsychiatric conditions, with special interest in the vegetative-endocrine diseases (schizophrenia, parkinsonism and epilepsy). They found disturbances of the coefficients of potassium and calcium, but it was not possible to correlate these with the vegetative nervous states. In a study of patients with functional neuroses Kylin [14] found five with hypercalcemia, twenty-seven with hypocalcemia and thirty-nine with normal blood calcium.

Timme [15] reported a group of cases in which he believed that deficiency in the utilization of calcium was related to glandular and behavior disorders. In nineteen of twenty-three cases a "low" blood (whole blood) calcium, varying from 5 to 8 mg. per hundred cubic

6. Henry, G. W., and Ebeling, W. W.: Blood Calcium and Phosphorus in Personality Disorders; The Effect of Ultraviolet Radiation, Arch. Neurol. & Psychiat. **16**:48 (July) 1926.

7. Armstrong, Edward, and Hood, Williamina: The Calcium Content of Serum in Mental Invalids, J. Ment. Sc. **73**:111 (Jan.) 1927.

8. Jacobi, W.: Ueber den Calcium- und Kalium- Blutserumspiegel bei katatonen Erregungszuständen, chronischen Schizophrenien und Melanocholien im Klimakterium, Monatschr. f. Psychiat. u. Neurol. **59**:130, 1925.

9. Scholberg, H. A., and Goodall, Edwin: The Phosphorus and Calcium Content of the Blood Plasma and Cerebrospinal Fluid in the Psychoses, J. Ment. Sc. **72**:51 (Jan.) 1926.

10. Tómasson, Helgi: Psychische Beeinflussung des Serumkalziumspiegels, Klin. Wchnschr. **3**:2055, 1924.

11. Klemperer, Edith: Untersuchungen über den Stoffwechsel bei manischen und depressiven Zustandsbildern: II. Veränderungen des Kalzium- und Kaliumspiegels des Gesamtblutes, Jahrb. f. Psychiat. u. Neurol. **45**:32, 1926.

12. Gullotta, S.: Il calcio del sangue e delle urine nei dementi precoci, Riv. di pat. nerv. **36**:572 (Nov.) 1930.

13. Futer, D. S., and Weiland, W. I.: Der Kalium-Calcium- Umsatz bei Nerven- und Geisteskrankheiten, Ztschr. f. d. ges. Neurol. u. Psychiat. **122**:811, 1929.

14. Kylin, Eskil: Der Gehalt des Blutes an Calzium und Kalium, Acta med. Scandinav., supp. 19, 1927, p. 1.

15. Timme, Walter: Pluriglandular Syndrome Involving Calcium Deficiency and Correlated with Behavior Disturbances, Arch. Neurol. & Psychiat. **21**:254 (Feb.) 1929.

centimeters, was found. Although other patients showing the same symptoms presented a "normal" blood calcium, since all the patients improved following the administration of calcium and parathyroid extract be believed that low utilization of calcium was the basic disturbance and that the behavioristic anomalies may belong in the same category, depending on the nonutilization of calcium by the nervous system, and that the same factors that bring about myotatic irritability in muscles also bring about untoward reactions in the nervous system. Since blood cells contain little or no calcium, the calcium content of whole blood is determined less by the concentration of calcium in either the cells or the serum than by the relative proportion of cells and serum in the blood. This fact makes difficult the clinical interpretation of the results of determinations of whole blood calcium (Peters and Van Slyke [16]). Values for whole blood calcium of from 5 to 8 mg. per hundred cubic centimeters are the normal values reported by most observers (Leiboff [17] and Rymer and Lewis [18]).

Since Rona and Takahashi,[19] in 1911, first showed that only a portion of the calcium of the serum is capable of diffusing through a colloid impermeable membrane a considerable bulk of evidence has accumulated in support of the view that the diffusible fraction, and perhaps only its ionized component, is concerned with the control of neuromuscular irritability.

Cameron and Moorhouse,[20] in 1925, suggested that the calcium of the cerebrospinal fluid represents the diffusible calcium of the plasma. Although since that time evidence of various types bearing on this point has been brought forward, opinion is still divided as to whether ultrafiltration wholly explains the presence of calcium in the cerebrospinal fluid.

Reports of studies of the calcium of the blood and the cerebrospinal fluid in mental disease are not lacking, but we found reports of only a few scattered instances in which the calcium of the blood and the cerebrospinal fluid was compared with that of an ultrafiltrate of the serum. Our series, in which these three determinations were made simultaneously,

16. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, vol. 1.

17. Leiboff, S. L.: Absence of Calcium in Human Red Blood Cell, J. Biol. Chem. **85**:759 (Feb.) 1930.

18. Rymer, M. R., and Lewis, R. C.: Studies on Calcium Content of Human Blood Corpuscles, J. Biol. Chem. **95**:441 (March) 1932.

19. Rona, P., and Takahashi, D.: Ueber das Verhalten des Calciums im Serum und über den Gehalt der Blutkörperchen an Calcium, Biochem. Ztschr. **31**:336, 1911.

20. Cameron, A. T., and Moorhouse, V. H. K.: The Tetany of Parathyroid Deficiency and the Calcium of the Blood and Cerebrospinal Fluid, J. Biol. Chem. **63**:687 (April) 1925.

consists of eighty patients in whose cases eighteen various neuropsychiatric diagnosis were made. In a previous communication [21] we showed that the calcium content of the cerebrospinal fluid in these cases is a close measure of the diffusible calcium content of the blood. It is now proposed to present the results of an attempt to relate the clinical findings in these patients to these chemical data. The distribution of the clinical conditions considered is shown in table 1. Worthy of comment is the high incidence (60 per cent) of vasomotor instability, which is reflective of autonomic imbalance. Among the cases most likely to be associated with neuromuscular irritability are those of constitutional psychopathic inferiority, psychopathic personality and behavior problems. Clinically this is borne out by the proportionately higher incidence of factors usually associated with "nervous instability." Eighteen (23 per cent) of the total group of patients presented enuresis (in all instances there was persistent enuresis past the age of 6, except in 2 cases, in which it was present only until the age of 4). Twelve (67 per cent) of the patients with enuresis belonged to the group just mentioned. It has been shown by one of us and Goodman [22] that enuresis is a valuable indicator of the psychobiologic reactivity or an individuation of an ill balanced personality. Five of the nine left-handed patients, four of the six who had enuresis and were also left-handed, three of the six who had a history of sensitization, five of the six who had temper tantrums and the three with a positive Chvostek sign belonged to this special group (table 1).

In none of the different diagnostic groups were abnormal calcium findings obtained (table 2). Of course, many of the groups were very small. However, even in the group of twenty-three patients with conditions diagnosed as constitutional psychopathic inferiority, psychopathic personality and behavior problems, with definite evidences of neuromuscular irritability, one finds no corroboration of the thesis of Timme.[15] When the calcium findings of the patients who showed the various indicators of so-called nervous instability are arrayed according to these symptoms no essential differences from the normal are noticed. We could not confirm the findings of Macciotta,[23] who in seventeen cases of essential enuresis (manifestations of spasmophilia) reported more or less marked galvanic excitability, hypocalcemia and a slight diminution of the ionic concentration of blood calcium, associated in some cases

21. Searle, O. M., and Michaels, J. J.: A Comparison of the Calcium Content of Human Cerebrospinal Fluid with That of an Ultrafiltrate of Serum, Am. J. Physiol. **103**: 455 (Feb.) 1933.

22. Michaels, J. J., and Goodman, S. E.: Incidence and Intercorrelations of Enuresis and Other Neuropathic Traits in So-Called Normal Children, Am. J. Orthopsychiat. **4**:79, 1934.

23. Macciotta, G.: Spasmophilic Forms of Enuresis in Children, Pediatria **38**:1145 (Nov. 1) 1930.

TABLE 1.—*General Survey of Patients with Various Clinical Conditions Distributed According to Diagnosis*

Diagnosis	Number of Patients	Average Age, Years	Sex		History of Convulsions	Spasms in Infancy	Sensitization	Delirium with Fever	Temper Tantrums	Enuresis	Left-Handedness	Enuresis and Left-Handedness	Constitutional Anomalies	Neurologic Disorders	Positive Chvostek Sign	Secondary Anemia	Albuminuria	Increased Protein in Spinal Fluid	Type			Vasomotor Instability	Endarteritis	Mean Systolic Pressure	Mean Diastolic Pressure	Mean Pulse Pressure	Mean Intelligence Quotient
			Male	Female															Asthenia	Athletic	Pyknic						
Schizophrenia	15	23.7	13	2	1	..	..	..	..	1	..	..	1	..	..	1	2	2	10	5	..	11	..	124.0	75.0	49.0	74.0
Paranoid disorder	9	44.7	6	3	1	..	1	1	..	..	..	..	1	..	..	3	1	..	3	2	4	3	4	128.0	83.0	45.0	83.0
Manic-depressive psychosis	4	31.0	..	4	..	..	..	..	1	2	1	1	..	..	..	2	1	..	2	1	..	2	1	116.0	75.0	41.0	90.0
Involutional melancholia	1	53	..	1	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	1	150.0	98.0	52.0	
Psychoneurosis	9	35.2	8	1	..	..	1	..	..	1	..	..	1	..	..	1	1	..	3	1	4	6	4	120.0	75.0	45.0	85.0
Constitutional psychopathic inferiority	11	17.5	3	8	..	1	3	1	5	8	2	2	3	..	3	2	1	..	6	1	2	9	..	114.0	71.0	43.0	85.0
Psychopathic personality	5	23.4	4	1	..	..	..	..	..	..	1	..	..	..	..	2	..	..	3	..	..	3	..	118.0	82.0	36.0	84.0
Behavior problem	7	23.1	6	1	2	..	..	..	..	4	2	2	..	..	..	1	1	2	4	2	1	5	..	119.0	70.0	49.0	84.0
Dementia paralytica	5	43.6	3	2	..	..	1	..	..	..	1	..	..	..	..	..	..	..	3	..	..	..	5	104.0	69.0	45.0	
Psychosis with syphilis of the central nervous system	1	54.0	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	143.0	65.0	78.0	
Toxic psychosis	2	41.0	2	..	..	..	..	1	..	1	1	1	1	..	..	..	..	..	..	..	2	1	1	127.0	86.0	41.0	80.0
Symptomatic psychosis	2	19.5	2	..	..	..	..	..	..	..	..	..	..	1	..	1	..	..	2	..	..	2	..	105.0	75.0	30.0	
Epilepsy	1	20.0	..	1	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	1	..	..	120.0	65.0	55.0	55.0
Psychosis with organic disease of the brain	2	50.0	2	..	..	..	..	..	..	..	1	..	..	1	..	..	..	1	..	..	..	2	2	125.0	82.0	43.0	73.0
No psychosis; disease of the central nervous system	1	20.0	..	1	..	..	..	..	..	..	..	..	..	1	..	..	1	..	..	..	..	1	..	128.0	85.0	43.0	
Psychosis with mental deficiency	2	27.0	1	1	..	..	..	..	..	1	..	..	..	..	..	..	..	..	2	..	..	1	..	115.0	77.0	38.0	62.0
Mental deficiency without psychosis	3	29.0	1	2	..	..	..	..	..	..	..	..	1	..	..	2	1	..	2	..	1	2	1	117.0	74.0	42.0	55.0
Total	80	30.0	52	28	4	1	6	3	6	18	9	6	8	4	3	15	10	5	40	12	15	48	20	120.8	75.8	45.2	81.6

TABLE 2.—*Relation of Diagnosis to the Calcium of the Blood Serum, Spinal Fluid and Filtrate of Serum with Their Ratios* *

Diagnosis	No. of Patients	Serum Calcium		Cerebrospinal Fluid Calcium		Cerebrospinal Fluid Calcium / Serum Calcium Percentage		Filtrate Calcium		Filtrate Calcium / Serum Calcium Percentage		Filtrate Calcium / Cerebrospinal Fluid Calcium Percentage	
		Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
Schizophrenia	15	9.8-10.7	10.2	4.5-5.1	4.8	44-50	47	4.1-6.0	5.0	40-61	49	84-133	104
Paranoid disorder	9	9.1-11.2	10.2	4.6-5.1	4.9	43-56	48	4.3-6.5	5.4	42-61	53	92-135	111
Manic-depressive psychosis													
Manic phase	2	8.9- 9.6	9.3	4.6-4.7	4.7	49-52	51	4.7-5.0	4.9	49-56	53	100-109	105
Depressed phase	2	10.6-10.7	10.7	4.6-4.8	4.7	43-45	44	4.6-4.7	4.7	43-44	44	98-100	99
Involutional melancholia	1	.....	9.9	.....	4.7	.....	47	.....	4.3	.....	43	.....	91
Psychoneurosis	9	9.7-11.6	10.5	4.6-5.4	5.0	43-56	47	4.9-5.4	5.2	47-55	50	98-118	106
Constitutional psychopathic inferiority (*a*)	11	9.3-10.8	10.1	4.5-5.0	4.8	45-50	48	3.9-6.2	5.1	41-60	50	85-129	106
Psychopathic personality (*b*)	5	9.8-10.4	10.0	4.5-4.8	4.7	45-48	46	4.5-5.7	5.2	45-57	52	96-125	111
Behavior problem (*c*)	7	9.4-10.7	10.0	4.4-5.0	4.8	43-51	48	4.4-5.5	4.9	45-56	49	94-112	103
(*a*) + (*b*) + (*c*)	23	9.3-10.8	10.1	4.4-5.0	4.8	43-51	47	3.9-6.2	5.0	41-60	50	85-129	106
Dementia paralytica	5	9.2-11.2	10.3	4.8-5.3	5.1	45-50	48	4.7-6.0	5.3	48-65	52	96-118	105
Psychosis with syphilis of the central nervous system	1	.....	10.6	.....	5.0	.....	47	.....	5.2	.....	49	.....	104
Toxic psychosis	2	10.1-10.2	10.2	4.8-5.0	4.9	48-49	49	4.6-4.9	4.8	45-49	47	92-102	97
Symptomatic psychosis	1	.....	9.8	.....	4.8	.....	49	.....	5.4	.....	55	.....	113
Epilepsy	1	.....	9.9	.....	4.5	.....	45	.....	4.7	.....	47	.....	104
Psychosis with organic disease of the brain	2	9.7- 9.9	9.8	4.6-5.0	4.8	46-52	49	4.7-5.0	4.9	48-50	49	94-109	102
No psychosis; disease of the central nervous system †	1	.....	9.8	.....	4.7	.....	48	.....	4.1	.....	42	.....	87
Psychosis with mental deficiency	2	10.8-10.9	10.9	4.9-5.2	5.1	45-48	47	4.8-5.2	5.0	44-48	46	98-100	99
Mental deficiency without psychosis	3	10.1-10.7	10.3	4.9-5.2	5.1	49-51	50	4.7-7.0	5.7	47-65	55	96-135	110
Total	80	8.9-11.6	10.2	4.4-5.4	4.8	43-56	48	3.9-7.0	5.1	40-65	50	84-135	105

* All concentrations are expressed in milligrams per hundred cubic centimeters.

† Multiple neuritis.

with evidences of mechanical hyperexcitability. Handowsky [24] was unable to find any difference between the range of serum calcium values in adults with a positive Chvostek sign and that in persons without this sign. Our four patients with a history of convulsions in infancy had the highest ratio (114.5) of filtrate calcium to spinal fluid calcium, while the only patient with epilepsy had a ratio of 104 (table 2). The studies of Pottenger [25] and Cantarow [26] apparently demonstrated the relationship of the calcium content of the cerebrospinal fluid to autonomic imbalance, asthma, mucous colitis and angioneurotic edema. Our six patients with a history of sensitization displayed none of the variations that Cantarow [26] reported, but he dealt with more cases, and these patients presented the symptom at the time of the chemical examination.

An attempt to relate the calcium findings to body type, determined according to either the Wertheimer-Hesketh [27] index or the weight-height index (weight in pounds divided by height in inches) of Greenwood,[28] confirmed the results obtained by Herzfeld and his collaborators,[29] who in a critical review of the literature found no relationship between constitution (as expressed in body type) and serum calcium.

Signs of vasomotor instability, including cold clammy hands, cyanosis and blotchiness of the skin of the extremities, were noted in each case, and an attempt was made to specify the degree as mild, moderate or marked. Regardless of the degree, we were unable to find any significant difference between the figures for calcium for these patients and those for subjects who did not show these symptoms.

It seemed possible that the blood pressure might be related to vascular conditions that would influence the permeability of the hematoencephalic barrier. However, although our subjects showed variations in blood pressure over a considerable range (systolic, from 85 to 168; diastolic, from 45 to 116; pulse pressure, from 22 to 80) we were not

---

24. Handowsky, Ida: Der Calciumbestand des menschlichen Blutes bei Fehlen und bei Vorhandensein des Facialisphänomens, Jahrb. f. Kinderh. **91**:432, 1920.

25. Pottenger, F. M.: The Relationship of the Ion Content of the Cells to Symptoms of Disease with Special Reference to Calcium and Its Therapeutic Application, Ann. Clin. Med. **2**:187 (Nov.) 1928.

26. Cantarow, Abraham: The Diffusibility of Calcium in Bronchial Asthma and Allied Disorders and in Pulmonary Tuberculosis, Am. J. M. Sc. **179**:497 (April) 1930.

27. Wertheimer, F. I., and Hesketh, F. C.: The Significance of the Physical Constitution in Mental Disease, Medicine Monographs no. 10, Baltimore, Williams & Wilkins Company, 1926.

28. Greenwood, Arthur: The Health and Physique of School Children, Westminster, England, P. S. King and Son, 1913.

29. Herzfeld, Ernest; Lubowski, Helene, and Krüger, Reinhard: Die klinische Bedeutung des Serumkalkspiegels beim Menschen: Kritische Uebersicht (1923-1928), Folia haemat. **41**:73 (May) 1930.

TABLE 3.—*Relation of Various Indicators of Nervous Instability and Other Factors to the Calcium of the Blood Serum, Spinal Fluid and Filtrate of Serum, with Their Ratios* *

Condition	No. of Patients	Serum Calcium		Cerebrospinal Fluid Calcium		Cerebrospinal Fluid Calcium / Serum Calcium Percentage		Filtrate Calcium		Filtrate Calcium / Serum Calcium Percentage		Filtrate Calcium / Cerebrospinal Fluid Calcium Percentage	
		Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
History of convulsions	4	9.9-11.2	10.1	4.4-4.9	4.7	43-49	46	4.6-6.5	5.4	45-58	52	105-135	115
Spasms in infancy	1	.....	9.3	.....	4.7	.....	50	.....	5.0	.....	54	.....	106
Delirium with fever	3	10.0-10.2	10.1	4.8-5.1	5.0	48-50	49	4.9-6.2	5.5	49-61	54	102-121	110
Sensitization	6	9.8-10.8	10.4	4.8-5.1	5.0	46-49	48	4.5-5.8	5.2	46-54	50	94-116	103
Temper tantrums	9	8.9-10.8	10.1	4.5-5.0	4.7	44-52	48	4.5-5.8	5.2	45-57	52	98-125	110
Enuresis	18	9.5-10.9	10.1	4.5-5.4	4.9	45-56	48	3.9-6.2	5.1	41-61	50	85-133	104
No enuresis	62	8.9-11.6	10.2	4.4-5.3	4.8	43-56	49	4.1-7.0	5.1	40-65	50	84-135	103
Left-handedness	9	9.2-10.4	10.0	4.6-5.1	4.8	46-55	49	4.5-6.0	5.0	45-65	51	92-118	104
Right-handedness	71	8.9-11.6	10.2	4.4-5.4	4.8	43-56	48	3.9-7.0	5.1	40-65	50	84-135	105
Left-handedness and enuresis	6	9.6-10.4	10.1	4.6-5.0	4.9	46-49	48	4.5-5.5	4.9	45-56	49	92-112	100
Constitutional anomalies †	8	9.5-11.2	10.3	4.5-5.4	4.9	43-56	48	3.9-6.5	5.1	41-58	50	83-135	105
Neurologic disorders ‡	4	9.8-10.7	10.1	4.6-4.8	4.7	45-48	47	4.1-5.3	4.7	42-50	46	87-110	99
Positive Chvostek sign	3	9.3-10.2	9.9	4.5-4.9	4.7	45-50	48	4.8-5.0	4.9	48-54	50	102-107	105
Secondary anemia §	15	9.1-10.3	10.1	4.6-5.2	4.9	45-56	49	4.5-7.0	5.2	44-65	52	96-135	107
Albuminuria ‖	10	9.7-10.7	10.1	4.5-5.2	4.8	45-49	47	4.1-7.0	4.9	42-65	49	87-135	103
Increased protein in spinal fluid ¶	5	9.7-10.1	9.9	4.7-5.0	4.8	48-52	49	4.3-5.1	4.6	43-53	47	90-106	96

* All concentrations are expressed in milligrams per hundred cubic centimeters.

† Congenital nystagmus, infantile dentition, undescended testes, imperforate anus, webbing of toes, and constitutional hypoplasia.

‡ Multiple neuritis, hemiplegia and Volkmann's contracture.

§ Red blood cells, 3,350,000 to 4,460,000; hemoglobin, from 65 to 80 per cent.

‖ A persistent faint trace.

¶ Nissl-Esbach index above 2 in the absence of demonstrable disease of the central nervous system or other organic disease.

able to correlate these with the spinal fluid calcium content or with its ratio to the serum calcium content or to the calcium content of the ultrafiltrate. Weinstein and Weiss [30] likewise were unable to demonstrate changes in the calcium content of the circulating blood in cases of arterial hypertension. It is generally considered that the condition of the retinal arteries is indicative of the cerebral vascular status. Various degrees (slight, mild, moderate and well marked) of retinal endarteritis (changes in the intima and generalized contraction of the arteries with diminution of caliber) were determined in twenty of our subjects by Dr. C. W. Lepard of the University of Michigan Hospital. The majority of the patients with endarteritis belonged to the age groups above 40. Neither the group as a whole nor patients in whom the condition was well marked showed calcium findings significantly different from those of the other subjects.

It has been claimed that deviations from the normal have been found in the blood calcium of the feebleminded. Intelligence quotients were available for sixty of our patients. Most of these were graded by the Stanford revision of the Binet-Simon scale, but when this was impossible a Porteus maze test was performed. Although the range in quotients was fairly wide (from 46 to 122, with a mean of 81.6), we could discover no correlation between them and any of the calcium findings.

To make possible comparison of our figures with those of other workers who expressed their results in this manner, the permeability quotients—the ratio of blood serum calcium to cerebrospinal fluid calcium—for our patients are given in table 4. Fleishhacker and Scheiderer [31] accepted from 1.8 to 2.2 as the normal range for the calcium ratio. Our figures—1.62 to 2.33—show much less fluctuation than those of Rothschild and Malamud,[32] who reported a range of from 1.53 to 2.50 in cases of manic-depressive psychosis. They concluded that the blood-cerebrospinal fluid barrier acts differently toward bromides than toward calcium, sugar and chlorides. Thirty-three and three-tenths per cent of their subjects presented abnormal ratios of calcium. Our small group

30. Weinstein, A. A., and Weiss, Soma: The Significance of the Potassium-Calcium Ratio and of the Inorganic Phosphorus and Cholesterol of the Blood Serum in Arterial Hypertension, Arch. Int. Med. **48**:478 (Sept.) 1931.

31. Fleishhacker, Hans, and Scheiderer, Georg: Ueber die Permeabilitätsquotienten (P. Q.) für Calzium, Chlor (Gesamthalogene) und Brom und ihre gegenseitigen Beziehungen bei Endogenen Geisteskrankheiten, Monatschr. f. Psychiat. u. Neurol. **75**:346 (May) 1930.

32. Rothschild, D., and Malamud, William: The Blood-Cerebrospinal Fluid Barrier in Manic-Depressive Psychosis: Ratios of Distribution of Bromide, Calcium, Sugar and Chlorides, Arch. Neurol. & Psychiat. **26**:829 (Oct.) 1931.

with manic-depressive psychoses (four cases) and one patient with involutional melancholia gave ratios which were close to our mean (2.11).

It is Cantarow's belief that the ratio of diffused (spinal fluid) calcium to nondiffused (serum calcium minus spinal fluid) calcium is an expression of the distribution of calcium between the plasma and the tissues. In sixty-eight normal persons studied by him [33] this "diffusibility ratio" ranged from 82 to 115; in thirty-one patients with atopic

TABLE 4.—*Ratios of Spinal Fluid Calcium to Nondiffused Calcium and of Filtrate Calcium to Nondiffused Calcium, and Permeability Quotients*

Diagnosis	No. of Patients	Cerebrospinal Fluid Calcium: Serum Calcium-Cerebrospinal Fluid Calcium Percentage		Filtrate Calcium: Serum Calcium-Filtrate Calcium Percentage		Serum Calcium: Cerebrospinal Fluid Calcium	
		Range	Mean	Range	Mean	Range	Mean
Schizophrenia	15	78- 98	88	67-154	98	2.02-2.28	2.13
Paranoid disorder	9	75-127	93	72-155	114	1.62-2.33	2.08
Manic-depressive psychosis	4	77-107	90	77-128	95	1.94-2.30	2.13
Involutional melancholia	1	.....	90	.....	77	.....	2.11
Psychoneurosis	9	76-125	91	87-120	101	1.80-2.32	2.13
Constitutional psychopathic inferiority	11	80-102	92	70-151	103	1.98-2.24	2.10
Behavior problem	7	75-104	92	81-125	98	1.96-2.32	2.09
Psychopathic personality	5	82- 92	87	80-130	107	2.08-2.21	2.15
Dementia paralytica	5	81-124	99	91-188	114	1.81-2.24	2.03
Psychosis with syphilis of the central nervous system	1	.....	89	.....	96	.....	2.12
Toxic psychosis	2	91- 96	94	82- 94	88	2.04-2.10	2.07
Symptomatic psychosis	2	81- 96	89	98-123	111	2.04-2.23	2.14
Epilepsy	1	.....	83	.....	90	.....	2.20
Psychosis with organic disease of the brain	2	87-106	97	94-102	98	1.94-2.15	2.05
No psychosis; disease of the central nervous system	1	.....	92	.....	72	.....	2.08
Psychosis with mental deficiency	3	83- 95	90	80-189	120	2.06-2.20	2.12
Mental deficiency without psychosis	2	94-106	100	87-110	99	1.99-2.06	2.03
Total	80	75-127	91	67-188	102	1.62-2.33	2.11

and autonomic disorders it ranged from 68.9 to 400, 81 per cent of the subjects showing a ratio outside the determined normal range. Our group showed a range of from 75 to 127, with a mean of 91 (table 4); these figures are not strikingly different from Cantarow's figures for the normal range. When a similar comparison is made, using the serum filtrate calcium instead of the cerebrospinal fluid calcium (table 4), a wider range in the diffusibilty ratio—from 67 to 188, with a mean of 102—is obtained. The highest figures were obtained for patients with dementia paralytica and psychosis with mental deficiency. However, because of the smaller volumes available, the determinations of calcium in our

33. Cantarow, Abraham: Calcium Metabolism and Calcium Therapy, Philadelphia, Lea & Febiger, 1931.

ultrafiltrates are less reliable than those of cerebrospinal fluid calcium, and in a calculation of this kind any error enters at least twice. We question the significance of these large ratios.

Cantarow [33] reported from 45 to 55 per cent as the ratio of diffused (spinal fluid) calcium to total serum calcium for normal subjects. The ratio for our group was close to this, with a range of from 43 to 56 per cent and a mean of 48. When the filtrate calcium was used as the diffusible calcium we obtained a slightly wider range of values (from 40 to 65 per cent, with a mean of 50 [table 2]). Weston and Howard [34] found a ratio of 50 per cent (spinal fluid calcium-blood serum calcium) in seventeen cases of the manic phase of manic-depressive psychosis and of 51 per cent in ten cases of the depressive phase. Katzenelbogen and Goldsmith [35] found the calcium content of the cerebrospinal fluid equal to from 44 to 65 per cent of that of the blood serum in forty-two cases of organic psychosis, from 41 to 54 per cent in schizophrenia, from 48 to 56 per cent in manic-depressive psychosis and from 46 to 53 per cent in mental deficiency. They concluded that the calcium content showed the same tendencies as the bromide content in the same diseases but that the tendencies are less pronounced with regard to the diffusion of calcium from the blood to the cerebrospinal fluid.

CONCLUSIONS

1. In eighty patients with neuropsychiatric disorders in eighteen different diagnostic groups there were no significant abnormal findings in regard to the calcium of the cerebrospinal fluid, the blood serum or an ultrafiltrate of the serum or in regard to the ratios of these quantities to each other.

2. In patients with nervous instability, various somatic and neurologic deviations, vasomotor instability and retinal endarteritis, the calcium findings were not different from those in patients who did not present these conditions.

3. The constitutional type (asthenic, athletic or pyknic), weight-height index, sex, age, blood pressure and intelligence quotient could not be correlated with the calcium findings.

4. The ratios of diffused to nondiffused calcium and the permeability quotients were within normal limits.

---

34. Weston, P. G., and Howard, M. Q.: The Determination of Sodium, Potassium, Calcium and Magnesium in the Blood and Spinal Fluid of Patients Suffering from Manic-Depressive Insanity, Arch. Neurol. & Psychiat. **8**:179 (Aug.) 1922.

35. Katzenelbogen, Solomon, and Goldsmith, Harry: The Distribution of Calcium Between Blood and Cerebrospinal Fluid in Mental Diseases, Am. J. Psychiat. **11**:9 (July) 1931.

5. The lack of uniform methods preventing comparisons, the lack of consistent corroboration of chemical results, superficial experimental data and empirical reasoning to prove the relationship of calcium deficiency to neuropsychiatric disorders should leave this fascinating question open, but with the stimulus toward more coordinated laboratory and clinical studies. It seems strongly indicated that one obtain blood and spinal fluids simultaneously and study the interrelationship of the calcium partitions with the values for other substances in these fluids, especially the amounts of inorganic phosphates and other inorganic elements and of proteins and, above all, the potassium-calcium ratios. The intensive study of fewer cases, with repeated studies of individual cases to ascertain normal fluctuations, especially when the clinical manifestations may be evanescent and transitory, is desirable. Prolonged persistent studies throughout the various phases of an illness as it occurs in the evolution of a psychosis, and especially in epilepsy, are also necessary. A multidimensional point of view implying knowledge of the integration and intricate intercorrelations and interdependence of all the levels of the personality is essential for any valuable contribution in the realm of calcium metabolism in patients with neuropsychiatric disorders.

A PHARMACODYNAMIC INVESTIGATION OF THE AUTONOMIC NERVOUS SYSTEM IN SCHIZOPHRENIA

I. EFFECT OF INTRAVENOUS INJECTIONS OF EPINEPHRINE ON THE BLOOD PRESSURE AND PULSE RATE

H. FREEMAN, M.D.
AND
H. T. CARMICHAEL, M.D.
WORCESTER, MASS.

The frequency of clinical observation of cold, moist, cyanotic extremities, hypotension,[1] bradycardia and low rates of oxygen consumption[2] in schizophrenic patients has led many investigators to postulate in this psychosis an imbalance or dysfunction of the autonomic nervous system, generally with a predominance of the parasympathetic division.[3] Studies in recent years have shown that the schizophrenic psychosis is marked by certain displacements of metabolic levels of performance and, what is probably of greater importance, that the relationships among various functions are seriously abnormal.[4] As a result, the patients, although able to show approximately normal organic performance in most respects and under episodic test conditions, nevertheless, on more penetrating study, disclose an inability to make rapid, smooth adaptive responses to given situations. They show "organic clumsiness." Fine coordination of the metabolic ("vegetative") processes (homeostatic efficiency) is dependent in a large measure on the efficiency and prompt responsiveness of the autonomic nervous system. Accordingly, the logic of events now demands a searching study of the functional conditions of the various components of the autonomic apparatus. A beginning of such investigation has been made by a series of studies intended to extend knowledge of the reactions of schizophrenic patients

---

From the Research Service of the Worcester State Hospital and the Memorial Foundation for Neuro-Endocrine Research, with the collaboration of the Research Staff.

1. Freeman, H.; Hoskins, R. G., and Sleeper, F. H.: The Blood Pressure in Schizophrenia, Arch. Neurol. & Psychiat. **27**:333 (Feb.) 1932.

2. Hoskins, R. G., and Walsh, A.: Oxygen Consumption ("Basal Metabolic Rate") in Schizophrenia, Arch. Neurol. & Psychiat. **28**:1346 (Dec.) 1932.

3. Kanner, L.: The Adrenalin Blood Pressure Curves in Dementia Praecox and the Emotional Psychoses, Am. J. Psychiat. **8**:75 (July) 1918.

4. Hoskins, R. G., and Sleeper, F. H.: Organic Functions in Schizophrenia, Arch. Neurol. & Psychiat. **30**:123 (July) 1933.

to certain drugs that selectively influence the sympathetic or parasympathetic components of the autonomic system. The drugs we have used are epinephrine, ergotamine, atropine and physostigmine. The blood pressure and heart rate were used as criteria of the responses to these agents.

In the present paper only the results with epinephrine will be considered. A review of the literature on the effects of this drug on the blood pressure and the pulse rate in schizophrenia shows marked inconsistencies. Many investigators have found that in this psychosis the usual pressor response is diminished or absent.[3] Others have noted differences in the reaction among the various subtypes, the catatonic group, especially, showing the least effect.[5] There are still others, however, who have observed no differences between normal and schizophrenic persons in this respect.[6]

The contradictory nature of the results may have been due in part to the use by many investigators of the subcutaneous route, with its notorious variation in absorption;[7] to a lack of uniformity in dosage; to a failure to utilize the optimum timing of the reaction, which in a drug with as transient an action as epinephrine is all important, and to a lack of satisfactory normal standards.

MATERIAL

The study was made on seventy-two schizophrenic male patients, chosen on the basis of freedom from detectable organic disease, and on twenty-four normal male subjects, presumably in good health, who included members of the staff and employees of the Worcester State Hospital. The investigation on the patients was performed over an interval of two weeks, subsequent to the second period of intensive study of the so-called "seven month schedule."[8] The control subjects were tested following the completion of the study of the series of patients.

The tests were performed under basal conditions, after thirty minutes' rest in bed. The drug was administered intravenously in standard dosage of 0.05 mg. and so diluted that the appropriate quantity was contained in 1 cc. of physiologic solution of sodium chloride. In order to evaluate the emotional stimulus derived from the venipuncture and its possible effect on the cardiovascular apparatus, control injections of 1 cc. of physiologic solution of sodium chloride were administered.

The exact technic of the test was as follows: Control blood pressure and pulse rate readings were obtained. The median basilic vein was then punctured, and

5. Dawson, W. S.: A Study of the Endocrine-Autonomic Disorders of Dementia Praecox, J. Ment. Sc. **69**:182, 1923.

6. Northcote, M. L. M.: The Clinical Investigation of the Autonomic Nervous System in Schizophrenia, J. Ment. Sc. **75**:114, 1929.

7. Koppanyi, T.: The Effect of Subcutaneously Injected Epinephrine in Normal Human Subjects, Proc. Soc. Exper. Biol. & Med. **25**:744, 1928.

8. Hoskins, R. G.; Sleeper, F. H.; Shakow, D.; Jellinek, E. M.; Looney, J. M., and Erickson, M. H.: A Cooperative Research in Schizophrenia, Arch. Neurol. & Psychiat. **30**:388 (Aug.) 1933.

the solution injected as rapidly as possible. Immediately following this the pulse rate was counted for a full minute and every three minutes thereafter for thirty minutes. The blood pressure was taken in the thirty seconds elapsing after the pulse rate had been estimated on each occasion. Thus the pulse rate was obtained during the first minute after injection, from the third to the fourth minute, from the sixth to the seventh minute, etc.; the blood pressure was read at one and one-half, four and one-half and seven and one-half minutes, etc. In a supplementary series in one group of fourteen patients readings were taken every thirty seconds for ten minutes.

The results of the injections of physiologic solution of sodium chloride were essentially negative. The mean changes after injection were slight, and the variation in blood pressure and pulse rate in the majority of cases was entirely random, within the limits of the fluctuation occurring continuously in the circulatory apparatus. It became evident that the venipuncture, per se, had no significant influence on the emotional status of the patients, and consequently in no way altered the findings.

RESULTS

In chart 1 is shown the effect of epinephrine on the mean systolic blood pressure in the series of fourteen patients. Immediately following injection there is a sharp rise in the systolic pressure which attains a maximum in sixty seconds and then falls abruptly to reach its previous level in four and one-half minutes. As the first postinjectional reading on the blood pressure in the main study is made at one and one-half minutes, it is evident that these results do not portray the total reaction to the drug. Readings obtained from sixty to ninety seconds after injection show a fall in pressure of 17 mm. in this group. However, as the error is constant for both normal subjects and patients, unless a differential effect is assumed, the comparison is unaffected.

In the case of the diastolic pressure (chart 1) there is a similar type of response, except that the control level is reached in two and one-half minutes and then shows a slight decline with a subsequent rise to the initial value. Although the mean curve shows an initial rise, in the individual case the change may be quite different, frequently involving an initial fall with a subsequent rise or an initial elevation with a subsequent fall. In view of this variability of behavior, the problem arises as to whether the reading obtained at ninety seconds, in the main study, is truly representative of the maximum change. By means of a scatter diagram it was determined that these two readings bore a close relationship, and that consequently the first postinjectional reading on the diastolic pressure might be considered a true index of the maximum change.

The results of the general study are summarized in table 1, in which are recorded the maximum changes following the administration of epinephrine. In each subject this change occurred at the time of the first observation subsequent to the injection. In the case of the systolic pressure, all the responses were of a pressor nature with the exception

of those of one patient in whom no change occurred. In the psychotic subjects, the mean elevation in systolic blood pressure was 43.8 mm. with a variation of 19.3 mm. on either side in two thirds of the cases. The range was quite broad, extending from 0 to 99 mm. In normal persons the mean rise was 56.2 mm. with a similar standard deviation.

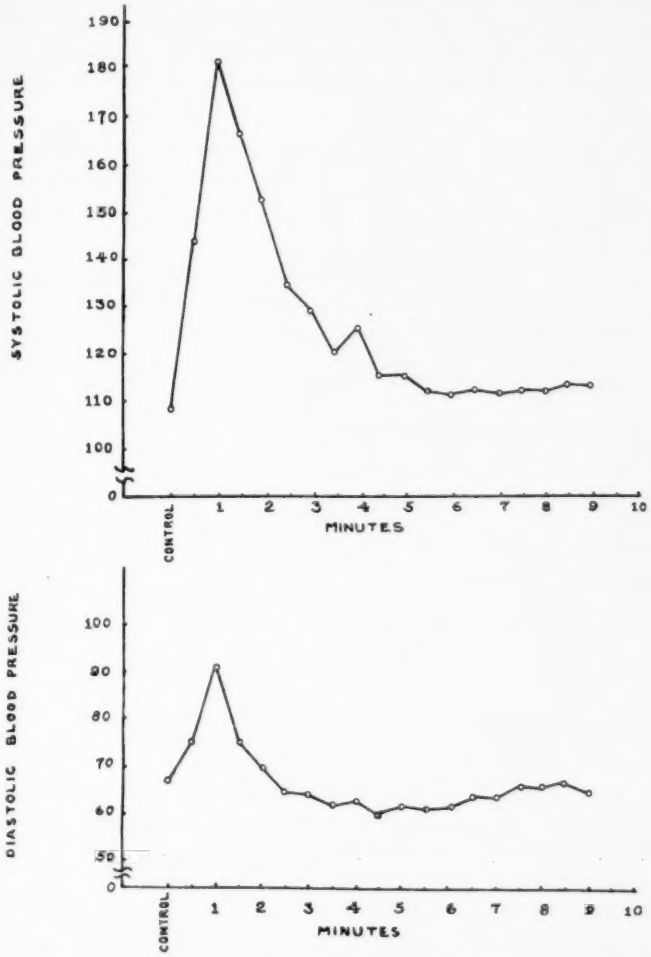


Chart 1.—Mean changes in the blood pressure after the administration of epinephrine to fourteen patients. The readings were taken at intervals of thirty seconds. The "control" reading was taken before the injection and all other readings after the injection at the time intervals noted at the bottom of the chart.

The range, however, was somewhat reduced at its lower extreme, extending from 22 to 93 mm. The difference between the means of the maximum elevations in the patients and normal persons—12.4 mm.—is statistically significant and indicative of an altered reactivity to the drug in the schizophrenic group. Despite this

diminution of response, the variability in the reaction among patients is quite similar to that among normal persons, as shown by the standard deviations. However, an analysis of the distributions presents several interesting differences. In chart 2 it is seen that while none of the normal subjects showed an elevation in systolic blood pressure of less than 20 mm., in approximately 8 per cent of the patients the change was less than this value. Furthermore, while in 62 per cent of the normal persons the systolic pressure was raised to a greater height than 50 mm., in only 41 per cent of the patients was this true. It should be noted that the slight responses of some of the patients were not due to errors in technic, for in each case a definite change was noted in either the diastolic pressure or the pulse rate.

In regard to the diastolic pressure, the situation is much more complex, the responses being both of a pressor and of a depressor nature. The mean change in the patients was an increase of 1.7 mm. In the normal subjects the difference was even less marked, the mean increase being 0.5 mm.

TABLE 1.—*Constants of Distributions Pertaining to Changes in Blood Pressure and Pulse Rate After the Injection of Epinephrine*

Variable	Minimum	Maximum	Range	Mean and σ M*	Standard Deviation and σ S.D.*
Change in systolic pressure (mm. Hg)					
Patients	0	99	99	43.8 ± 2.3	19.3 ± 1.6
Controls	22	93	71	56.2 ± 4.0	19.3 ± 2.8
Change in diastolic pressure (mm. Hg)					
Patients	−58	35	93	1.7 ± 1.9	15.9 ± 1.3
Controls	−18	26	44	0.5 ± 2.7	13.2 ± 1.4
Change in pulse rate (beats per min.)					
Patients	−7	53	60	13.6 ± 1.6	11.6 ± 1.0
Controls	1	29	28	16.3 ± 1.5	7.3 ± 1.1

* σM, standard error of mean; σS.D., standard error of standard deviation.

Despite the insignificant difference in the mean values, the individual reactions in many cases were quite marked, but in such a direction as essentially to cancel each other. A glance at the distributions of the maximum changes in the diastolic pressure (chart 3) reveals tendencies quite opposite to that of the systolic pressure, namely, a trend on the part of the patients to have positive changes, while in the case of the normal subjects, negative changes predominate. More specifically, while only 32 per cent of the patients showed a fall in the diastolic pressure, 58 per cent of the normal subjects changed in that direction.

Turning next to the pulse rate (chart 4), in the patients there was a mean increase of 13.6 beats, while in the normal subjects the mean value for the ventricular acceleration was 16.3 beats. The difference—2.7 beats per minute—between patients and control subjects, is not statistically significant, but it does not portray the entire picture. The standard deviations show that the normal subjects as a group exhibit less variability than the patients. Furthermore, while in the normal subjects all the changes are on the plus side and do not exceed a value of 30, in the patients 8.5 per cent show a slowing of the heart and in 10 per cent the change is greater than the maximum normal.

The exact meaning of this difference in type of reaction is not clear. The change in the ventricular rate after the injection of epinephrine is a diphasic reaction, there being initially a short period of acceleration followed by a phase of retardation with irregularities interspersed in both stages. Without the aid of graphic registration, one cannot separate the maximum changes in the two cycles, and consequently the total change over a minute represents a partial modification of the extent of the increase in rate. The second cycle is a vagal reflex, stimulated by the rise in blood pressure, and it is possible that the negative changes in the patients represent a predominance of vagal activity in the cardiovascular apparatus. The response of the autonomic nervous system depends to a certain extent

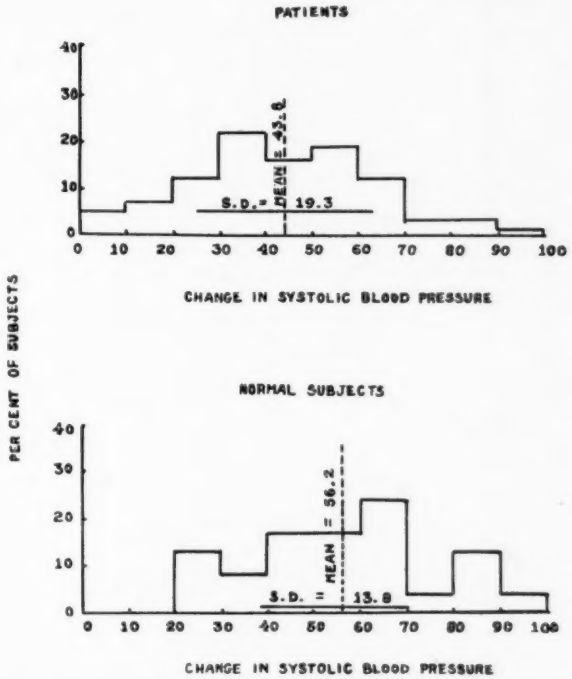


Chart 2.—Frequency distributions of maximum changes in systolic blood pressure after the injection of epinephrine.

on its initial state. Heymans and Laydon[9] found that with strong vagal tonus, epinephrine may stimulate the vagal center directly, provoking a bradycardia.

It must be emphasized at this juncture that we are dealing solely with group trends. Consideration of the problem of individual variability—which is considerable—must be deferred until adequate data have been secured.

The interrelationships of the various cardiovascular components were studied both before and after the administration of epinephrine. The systolic and diastolic pressures before injection in the patients exhibited a fair degree of relationship, the correlation coefficient being 0.57. In large groups of normal persons this

9. Heymans, C., and Laydon, A.: The Mechanism of the Hypertensive and Adrenaline Bradycardia, Compt. rend. Soc. de biol. **90**:966, 1924.

coefficient was 0.44. The higher value found in the patients seems to signify a more rigid obedience in the vascular mechanism to the operation of mechanical forces. The lesser correlation in the normal subjects may indicate a greater interference with this "mechanization" because of the presence of a more highly efficient sympathicosuprarenal system. No correlation was found between either phase of blood pressure and the pulse rate before injection, the physiologic processes influencing their course being apparently entirely separate.

The total effect produced by the injection of epinephrine in all three factors was apparently independent of the level of the control values. The parallelism

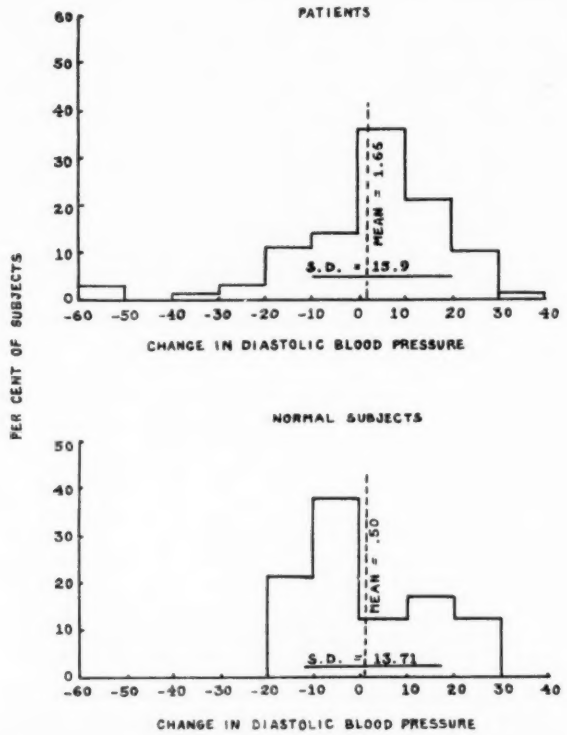


Chart 3.—Frequency distributions of maximum changes in diastolic blood pressure after the injection of epinephrine.

previously shown between the systolic and diastolic pressures in the patients was completely disrupted in this reaction, the amount of change in the systolic blood pressure bearing practically no relationship to that produced in the diastolic pressure. Again, the effect on the heart rate bore no relationship to the changes produced in the blood pressure.

Analysis of other physiologic variables showed a similar lack of interrelationship. No significant correlations were found in the reactions to epinephrine with the rate of oxygen consumption, although the variability of the latter determination in schizophrenia may have been sufficient to conceal any trend in this direction. Nutrition apparently played no part in the determination of the extent of the

reaction. The gastro-intestinal emptying time, the prolongation of which was an index of the efficiency of the sacral portion of the sympathetic division of the autonomic nervous system, also exhibited no correlation with the vascular changes produced by epinephrine. Age apparently had a slight influence in the extent of the reaction, the coefficient between the change in systolic pressure and age being —0.18; between the diastolic pressure and age, +0.26; and between the pulse rate and age, —0.23. The negativity of the trend as regards the systolic pressure and

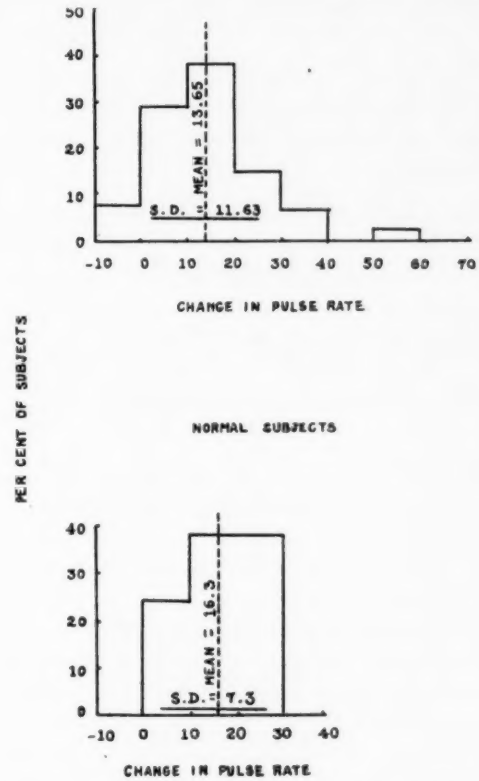


Chart 4.—Frequency distributions of maximum changes in pulse rate after the injection of epinephrine.

also the pulse rate may be due in part to the lessened efficiency of the cardiac musculature as a result of sclerotic processes, while the parallel course of the diastolic pressure may be attributed possibly to the superimposition of arteriosclerotic changes on an already relatively mechanized vascular apparatus. It is of interest that in the normal subjects the signs are reversed, although the values are so small that no conclusions can be drawn from them.

No correlations were found between the various changes and the period of hospitalization, so that the stabilization of environment obtained in the institution apparently had no effect on the degree of reactivity.

As various investigators have found differences in the reaction to epinephrine, in the various subclasses of schizophrenia,[10] an analysis was made of the findings in the different subtypes. The results, although based on relatively small samples, are summarized in table 2 for what they are worth. It is somewhat surprising that the greatest response—and one quite comparable to that of the normal—both in blood pressure and in pulse rate was obtained in the catatonic group, which is regarded in the literature as most frequently exhibiting a condition of vagotonia. The paranoid group, which is considered to show the least apparent degree of deterioration, showed a change similar to that of the entire schizophrenic group. The hebephrenic class was the chief contributor to the minus changes in the diastolic pressure.

Again, no correlation was found with the psychiatric status of the patient,[11] so that apparently the degree of adjustment to the environment had no effect on concerned were systolic blood pressure, pulse rate, gastro-intestinal the reaction to epinephrine.

To determine whether a syndrome of the nature of a hypothetic vagotonia existed in the patients, the relationships between four factors commonly associated with that concept were analyzed. The factors

TABLE 2.—*Average Maximum Change by Subgroups*

Groups of Subjects	Number	Change in Systolic, Mm. Hg	Change in Diastolic, Mm. Hg	Change in Pulse Rate
Paranoid	12	42.0	4.5	7.3
Catatonic	11	54.5	7.4	20.7
Hebephrenic	9	42.9	—10.0	15.0
Simple	3	31.0	—3.3	11.7
Mixed	6	22.0	8.2	13.8
Unclassified	17	46.2	—3.8	12.9
Indeterminate	13	47.8	8.9	13.4
Normal subjects	22	56.2	0.5	16.3

emptying time and rate of oxygen consumption. No characteristic combinations were found such as hypotension, bradycardia, decreased emptying time of the colon and low rate of oxygen consumption. We are, therefore, forced to conclude that the so-called vagotonic picture is not consistently present in schizophrenia, or that its definition must rest on grounds entirely different from those commonly accepted.

A complete estimation of the functional state of the autonomic nervous system is, on the basis of present knowledge, difficult to conceive. The existence of hypothetic syndromes of the nature of sympathicotonia or vagotonia has never been proved in clinical practice and seems even more doubtful in view of the lack of changes observed in completely sympathectomized animals under resting conditions.[12] In that investi-

10. Langfeldt, G.: The Endocrine Glands and Autonomic Systems in Dementia Praecox, Bergen, J. W. Eides, Boktrykkeri, 1926.

11. Erickson, M. H., and Hoskins, R. G.: Grading of Patients in Mental Hospitals as a Therapeutic Measure, Am. J. Psychiat. **11**:103 (July) 1931.

12. Cannon, W. B.; Newton, H. F.; Bright, E. M.; Menkin, V., and Moore, R. M.: Some Aspects of the Physiology of Animals Surviving Complete Exclusion of Sympathetic Nerve Impulses, Am. J. Physiol. **89**:84, 1929.

gation, removal of both sympathetic chains prevented the animal from responding properly in an emergency. In the schizophrenic patients, the situation is not comparable for the response to the stimulus is on the whole adequate, but when the necessity for action is removed the patient sinks to a subnormal level. It is clear, therefore, that the physiology of the schizophrenic patient does not fall easily into the class of hyposympathicotonia or vagotonia on the basis of analogy with animal experimentation. For an interpretation of its abnormalities, we must turn to other concepts.

Findings as regards the circulation time [13] and the systolic-diastolic relationship, as well as the results herein reported on the response to epinephrine, indicate a depression of the adjustment system in schizophrenic patients so that mechanical forces at work in the circulatory apparatus have freer than normal rein, in a measure unchecked by the niceties of neural regulation.

SUMMARY

In twenty-four normal male subjects and in seventy-two schizophrenic patients free from detectable organic disease, the reaction of the blood pressure and the pulse rate to the intravenous injection of 0.05 mg. of epinephrine was investigated. The following results were obtained:

1. The maximum change in blood pressure and pulse rate was attained within the first minute after injection.

2. The mean rise in systolic pressure in the schizophrenic patients was 43.8 mm. and in the normal subjects, 56.2 mm. The difference between these two values is statistically significant and indicative of a diminished reactivity to the drug in the psychotic group.

3. In the case of the diastolic pressure, the reaction was quite variable, and the mean change in both patients and normal subjects was slight. There was, however, a greater tendency for the patients to show a rise in the diastolic pressure.

4. In the patients the mean increase in pulse rate was 13.6 beats per minute and in the normal subjects, 16.3 beats. The difference is not significant, but in the distributions the patients showed a greater diversity of response and, in some cases, a slowing of the rate. This may possibly be attributed to the existence of a strong vagal tonus.

5. No correlation was found between the extent of the reaction and the initial levels.

6. No correlation was found between the reaction to epinephrine and the rate of oxygen consumption, nutritional index, schizophrenic

13. Freeman, H.: The Arm-to-Carotid Circulation Time in Normal and Schizophrenic Subjects, Psychiat. Quart. **8**:290 (April) 1934.

subclass, psychiatric status or emptying time of the colon. Age apparently had a slight effect in lessening the total degree of response.

7. No characteristic syndrome of autonomic imbalance—including the levels of blood pressure, pulse rate, basal metabolism and the emptying time of the colon—was found in schizophrenia.

8. Before the injection of epinephrine, the systolic and diastolic pressures in the patients exhibited a fair degree of relationship, the correlation coefficient being 0.57. After the injection of epinephrine, the association was almost totally disrupted, the coefficient being practically zero.

EXPERIMENTALLY PRODUCED CONVULSIONS

EFFECT ON THUJONE CONVULSIONS OF INSULIN AND OF VARIATIONS IN WATER CONTENT OF BRAIN

H. M. KEITH, M.B. (Tor.)
MONTREAL, CANADA

During the past five years, since the reports of Fay [1] and MacQuarrie [2] in regard to the relationship of the water balance of the body to the occurrence of epileptiform seizures, there has been a great deal of interest in hydration, dehydration and the water content of the tissues. In previously reported experiments [3] I have shown that rapid dehydration decreases the rabbit's susceptibility to experimental convulsions. The present paper deals with attempts to increase this susceptibility to convulsions by inducing "hydration" of the brain tissue and by the use of insulin and the induction of hypoglycemia.

MacQuarrie carried out experiments on epileptic children, giving them large amounts of water by mouth, accompanied in some cases by posterior lobe pituitary solution. He noted an increase in the number and severity of the epileptic attacks when the water was retained in the body in excessive amounts, and a reduction in the number, or a total disappearance, of the seizures when the intake and output of water were at a low level. He suggested that there is a disturbance in the regulation of water exchange in epilepsy, with possible hydration of the brain tissues. Both MacQuarrie and Fay recommended restriction of the intake of water in treating patients with epilepsy and reported some success in using this dehydration method.

In the present study the experimental convulsions were produced, as described previously,[3] by the intravenous injection of thujone emulsified in acacia. Thujone is the chief constituent of the volatile oil of absinth (wormwood) and has the formula $C_{10}H_{16}O$. Absinth was first

---

From the Department of Neurology and Neurosurgery, McGill University, Montreal.

1. Fay, Temple: Some Factors in the "Mechanical Theory of Epilepsy" with Especial Reference to Influence of Fluid, and Its Control, in Treatment of Certain Cases, Am. J. Psychiat. **8**:783 (March) 1929.

2. MacQuarrie, Irvine: Epilepsy in Children: The Relationship of Water Balance to the Occurrence of Seizures, Am. J. Dis. Child. **38**:451 (Sept.) 1929.

3. Keith, H. M.: The Effect of Various Factors on Experimentally Produced Convulsions, Am. J. Dis. Child. **41**:532 (March) 1931.

used as a convulsant by Marcé [4] in 1864. Thujone has been used by Cobb,[5] Florey,[6] Sparks [7] and Lennox, Nelson and Beetham [8] and by me. In the experiments already reported rabbits were used as the test animals, and because of the irregularity in the response of the individual rabbits each experiment was carried out on a group of six or more animals and the results were treated statistically as suggested by Lennox, Nelson and Beetham. In addition, it was found necessary to use animals not previously inoculated or those that had not had injections for at least a week. The thujone was given as a 1 per cent emulsion in 6 per cent acacia, the minimal convulsant dose being from 0.35 to 0.4 cc. per kilogram of body weight. One-half this dose, or 0.2 cc. per kilogram, was used to determine an increased susceptibility to the drug. It was found that of sixteen rabbits given this amount only 18.7 per cent responded with convulsions (table 1).

Studies of water intoxication had previously been made by Rowntree [9] and his co-workers, who showed that convulsions could be pro-

TABLE 1.—*Thujone (1 per Cent) Necessary to Produce Convulsions in Normal Rabbits*

Thujone, Cc. per Kg. of Body Weight	Rabbits Inoculated	Convulsions	
		Number of Rabbits	Per Cent
0.2	16	3	18.7
0.35—0.4	19	19	100

duced by the oral administration of large amounts of water, with or without the subcutaneous injection of solution of posterior lobe pituitary.

Misawa [10] studied the effects of water intoxication in rabbits and found that there was a reduction of chloride in all tissues of the body

4. Marcé: Note sur l'action toxique de l'essence d'absinthe, Compt. rend. Acad. d. sc. **58**:629, 1864.

5. Cobb, S.: Case of Epilepsy with General Discussion of Pathology, M. Clin. North America **5**:1403 (March) 1922.

6. Florey, A.: Action of the Convulsant Thujone, J. Path. & Bact. **28**:645 (Oct.) 1925.

7. Sparks, Irving: Experimental Studies of Epileptic Convulsions, Arch. internat. de pharmacodyn. et de thérap. **33**:460, 1927.

8. Lennox, W. G.; Nelson, R., and Beetham, W. P.: Studies in Epilepsy; Factors Affecting Convulsions Induced in Rabbits, Arch. Neurol. & Psychiat. **21**: 625 (March) 1929.

9. Rowntree, L. G.: The Water Balance of the Body, Physiol. Rev. **2**:116 (Jan.) 1922. Larson, E. E.; Weir, J. F., and Rowntree, L. G.: Studies in Diabetes Insipidus, Water Balance and Water Intoxication: Study I, Arch. Int. Med. **29**:306 (March) 1922.

10. Misawa, H.: Ueber das Wesen der sogenannten Wasserintoxication, Jap. J. M. Sc. Tr. (sect. VIII: Int. Med., Pediat. & Psychiat.) **1**:355 (Dec.) 1927.

except the liver. He found an increase in the water content of all the tissues examined. He believed that the symptoms of water intoxication were dependent on the reduction of inorganic salts in the tissues rather than on the increase of water. Manchester [11] found, in children, that with the retention of water following the administration of pitressin there was a large increase in the urinary excretion of sodium and chloride. Smyth, Deamer and Phatak,[12] in a study of water intoxication, in 1933, demonstrated that the convulsions shown by dogs given distilled water were closely associated with the loss of chloride by way of gastric secretion, with a resulting alkalosis, and were not directly dependent on water retention in the body.

On the other hand, Bridge and Iob,[13] in 1931, noted that the elimination of sodium chloride during fasting was coexistent with improvement in patients with epilepsy. They expressed the belief that the elimination of sodium and extracellular water might be, in part, responsible for the beneficial effect of both fasting and the ketogenic diet. In a careful study of the total exchange of water, sodium, potassium and nitrogen in epilepsy, Byrom,[14] in 1932, made observations which showed that spontaneous epileptic convulsions were not preceded by any alteration in the total exchange of these four substances. He pointed out that "convulsions might occur at a low level and yet be absent at a relatively higher level of tissue hydration." He believed that the convulsion was not a simple function of the degree of hydration of the tissues. Cobb [15] and his co-workers have shown that restriction of the intake of water did not appreciably lower the spinal fluid pressure, nor did drinking large amounts of water raise it. They therefore concluded that the undoubted beneficial effect of water restriction in some epileptic patients and the increase in seizures after drinking large amounts of water in others were not the result of changes in intracranial pressure.

As has been mentioned, I have shown that rabbits subjected to rapid dehydration by means of the intravenous injection of concentrated sugar solutions are definitely less susceptible to thujone convulsions than are normal rabbits. I have also shown that if rabbits are given

---

11. Manchester, R. C.: Influence of Posterior Pituitary Extracts on Mineral and Water Exchange in Children, Proc. Soc. Exper. Biol. & Med. **29**:1717, 1932.

12. Smyth, F. C.; Deamer, W. C., and Phatak, N.: Studies in So-Called Water Intoxication, J. Clin. Investigation **12**:55 (Jan.) 1933.

13. Bridge, E. M., and Iob, L. V.: Mechanism of Ketogenic Diet in Epilepsy: Preliminary Report of Work in Progress, Am. J. Psychiat. **10**:667 (Jan.) 1931; Mechanism of Ketogenic Diet in Epilepsy, Bull. Johns Hopkins Hosp. **48**:373 (June) 1931.

14. Byrom, F. B.: A Study of the Total Exchange of Water, Sodium, Potassium and Nitrogen in Epilepsy, Quart. J. Med. **25**:289 (April) 1932.

15. Cobb, S.: Causes of Epilepsy, Arch. Neurol. & Psychiat. **27**:1245 (May) 1932.

large amounts of water by stomach tube and a single injection of pitressin their susceptibility to thujone convulsions is increased slightly and there is some increase in the amount of water in the brain tissues.[16] I believed that this susceptibility could be further increased by repeated administrations of water and pitressin. The method consisted in giving, by stomach tube, an amount of water equal to 5 per cent of the body weight every one and one-half to two hours, each time injecting subcutaneously 0.1 cc. of pitressin. This procedure caused prostration and spontaneous convulsions in seven rabbits, much as described by Rowntree, and it was found that six of the seven (85.7 per cent) had severe convulsions after one-half the convulsant dose of thujone. There was an increased amount of water in the brain, as the brain solids in these animals averaged 19.8 ± 0.24 per cent (normal, 21.6 ± 0.07 per cent).

TABLE 2.—*Influence of Fluid and Pitressin on Rabbit's Susceptibility to Thujone Convulsions*

Substances Given	Amount, Cc.	Total Number of Animals	Number with Spontaneous Convulsions	Thujone, Cc. per Kg.	With Convulsions		Brain Solids, per Cent
					Number	Per Cent	
Pitressin (subcutaneously) Distilled water (by stomach tube)	0.1 180 to 500	7	7	0.2	6	85.7	19.81±.24
Pitressin (subcutaneously), 10 doses	0.1	8	0	0.2	3	37.5	21.3 ±.21
Hypotonic saline solution (0.45 per cent intravenously)	150 to 500	13	0	0.2	2	15.7	19.17±.14
Distilled water (by stomach tube)	560 to 850	6	2	0.2	4	66.8	19.4
Controls (43 rabbits)							21.6 ±.07*

* This figure is in close agreement with the figures given by Barbour (J. Pharmacol. & Exper. Therap. **43**: 147, 1931) for the solid content of the rabbit's brain, and by Greene (personal communication) for the solid content of the rat's brain. It is slightly higher than the figures given by Misawa.[10]

A control experiment was carried out in the following manner: Each of twelve rabbits was given an intravenous injection of 0.45 per cent saline solution (distilled water was injected into two others) to produce edema of the brain tissue, after the method of Kubie.[17] This procedure increased the amount of water in the brain even more than that used in the preceding group, the percentage of solids being 19.17 ± 0.14, but it did not increase the animal's susceptibility to convulsions, as only two of thirteen rabbits (15.4 per cent) responded to the test dose of thujone (table 2). This finding does not agree with

16. Keith, H. M.: Factors Influencing Experimental Convulsions, Arch. Neurol. & Psychiat. **29**:148 (Jan.) 1933.

17. Kubie, L. S.: Intracranial Pressure Changes During Forced Drainage of the Central Nervous System: The Hydration Factor in the Intracranial Pressure in Health and Disease, Association for Research in Nervous and Mental Disease, ser. research publ., 1927, vol. 8, p. 68, Baltimore, Williams & Wilkins Company, 1929.

that of Elsberg and Pike,[18] who gave distilled water intravenously and found that this decreased the minimal convulsant dose of absinth.

Pitressin alone was not responsible for the pronounced increase in liability to convulsions, as shown by the following experiment: Each of eight rabbits was given ten subcutaneous injections of pitressin at hourly intervals. After the final injection each was given a one-half convulsant dose of thujone. Three (37.5 per cent) of the animals responded with convulsions, a figure a little higher than the percentage in the control group but not comparable with the percentage in the group given pitressin and water. Moreover, these animals did not have an increase in the water content of the brain, the percentage of solids being 21.3 ± 0.21 (controls, 21.6 ± 0.07).

The administration of distilled water by stomach tube without the injection of pitressin did, however, increase to a greater extent the animal's susceptibility to convulsions. Of six rabbits given from 580 to 850 cc. of distilled water over periods of from six to twelve hours, four, or 66.6 per cent, had convulsions after one-half the convulsant dose of thujone, but it was noted that the severity of the convulsions was less than in animals given water and pitressin. The water content of the brain in the former group was as great as, or slightly greater than, in the latter, and in both groups was considerably greater than in normal animals.

From these experiments it is therefore evident that when repeated doses of pitressin are given to rabbits and at the same time large amounts of water are given by stomach tube, prostration and convulsions occur, as in human patients, and the rabbits are rendered more susceptible to thujone. That this is not due to the increased amount of water in the brain is shown by the fact that rabbits given hypotonic saline solution intravenously did not have spontaneous convulsions and were not more susceptible to thujone, yet the water content of the brain was as great as, or greater than, that of the former group. Whatever may be the factor that increases the animal's susceptibility to convulsions, it is evidently not the increase in the water content of the brain alone, nor is it the injection of pitressin alone. The giving of large amounts of water by stomach tube produces some change, however, and pitressin given at the same time appears to increase the effect of this change.

It is well known that the administration of insulin, with resulting hypoglycemia, causes severe convulsions in rabbits. It was previously reported [16] that rabbits treated in this way were not more susceptible to thujone convulsions. These rabbits, however, were given only 3 units of insulin, and the blood sugar was not reduced below 38 mg. per hun-

18. Elsberg, C. A., and Pike, E. H.: Influence of a General Increase or Diminution of Intracranial Pressure upon the Susceptibility of an Animal to Convulsions, Am. J. Physiol. **76**:593, 1926.

dred cubic centimeters, nor did the animals have spontaneous convulsions. The experiment was repeated, from 4 to 15 units of insulin being given to each of nine fasting rabbits. Eight of the nine had spontaneous convulsions within two and one-half hours. Five of the eight when given one-half the convulsant dose of thujone had definite convulsions. The blood sugar in four of these rabbits was below 25 mg. per hundred cubic centimeters and in one was 34 mg. The amount of water in the brains of these rabbits was determined and was found to be greater than in the normal controls (table 3). The mechanism of hypoglycemic convulsions is not as yet properly understood, but from the experiment described it is evident that insulin and hypoglycemia make the rabbit somewhat more susceptible to thujone convulsions. Behrendt and Hopmann [19] and Waltner [20] have demonstrated that hypo-

TABLE 3.—*Rabbits Given Insulin Followed by One-Half the Convulsant Dose of Thujone*

Rabbit Number	Weight, Kg.	Insulin, Units	Interval, Hours	Spontaneous Convulsions	Convulsions after Thujone*	Brain Solids, per Cent	Blood Sugar, Mg. per 100 Cc.
P 79	1.8	4	2½	+	3	....	2
P 106	1.7	5	2	+	2	19.7	23
P 107	2.9	7	1¾	+	0	19.5	44
P 108	1.9	5	2	+	0	19.0	30
P 109	2.2	12	2½	0	0	....	37
P 117	3.0	15	2½	+	4	....	34
P 220	2.8	15	1½	+	1	....	20
P 221	1.6	10	2	+	2	....	25
P 226	1.6	10	2	+	0	....	20
Average						19.4	
Controls						21.6±.07	

* Convulsions graded from 1 to 4 according to severity.

glycemia is associated with an increased irritability of nerve or muscle tissue to galvanic stimuli, and this may be sufficient to allow the moderately increased response to thujone. Jordan [21] stated that hypoglycemic convulsions may be prevented in certain groups of muscles by section of their nerve supply, even when convulsions occur in other groups. This indicates that the increased irritability is in the nervous system.

SUMMARY AND CONCLUSIONS

1. The administration of large amounts of water by stomach tube, accompanied by repeated subcutaneous injections of pitressin, causes spontaneous convulsions in rabbits, with increase in the water content

19. Behrendt, H., and Hopmann, R.: Ueber nichttetanoide Erregbarkeits-Veränderungen, Klin. Wchnschr. **3**:2233, 1924.

20. Waltner, K.: Insulin und galvanische Erregbarkeit, Klin. Wchnschr. **4**: 168, 1925.

21. Jordan, W. R.: Epilepsy and Convulsions in Diabetes, Arch. Int. Med. **52**:664 (Nov.) 1933.

of the brain, and makes them much more susceptible to thujone convulsions.

2. Pitressin alone, given in repeated subcutaneous injections, does not increase the water content of the rabbit's brain but does increase to a slight extent the animal's susceptibility to thujone convulsions.

3. Distilled water given by stomach tube in large amounts increases, to some extent, the susceptibility of the rabbit to thujone convulsions and, to a considerable extent, the water content of the brain.

4. The production of a maximal increase in the water content of the rabbit's brain by means of intravenous injection of hypotonic solution of sodium chloride does not increase the animal's susceptibility to thujone convulsions.

5. The production of insulin hypoglycemia to the point at which spontaneous convulsions occur makes rabbits more susceptible to thujone convulsions, and there is some increase in the water content of the brain accompanying this procedure.

6. Hypoglycemic convulsions and convulsions produced by the administration of water, or water and pitressin, do not inhibit the convulsant action of thujone.

7. Whatever the factor may be that increases the animal's susceptibility to convulsions, it is evidently not the increase in the water content of the brain.

CHOKED DISK AND PAPILLITIS

DIFFERENTIAL DIAGNOSIS BY THE PROTEIN CONTENT OF THE AQUEOUS

ELIAS SELINGER, M.D.
CHICAGO

It is well known that, in spite of the characteristic ophthalmoscopic findings, the clinical differentiation of papilledema and papillitis presents at times great difficulties. By definition, papilledema, or choked disk, is a noninflammatory swelling of the optic nerve head, while papillitis, also called neuroretinitis, is an inflammatory swelling of the disk and surrounding retina. More than 90 per cent of cases of papilledema are a result of increased intracranial pressure. This increased pressure, if unchecked, may lead not only to blindness but even to death. In cases of tumor or abscess of the brain in which the lesion cannot be localized and for that reason cannot be removed, or when the increased pressure is due to other causes, decompression is absolutely indicated if the peripheral visual fields begin to show constriction, and if medical management, such as the administration of hypertonic salt solutions or of mercury and iodides (even in nonsyphilitic cases), fails to bring relief from the increased intracranial pressure. If the choking of the disk is permitted to continue too long, blindness inevitably results. Decompression, on the other hand, is of no avail if the swelling of the optic nerve head is on the basis of an inflammatory process of the optic nerve, its sheaths or the surrounding tissues. It is therefore admittedly of great importance to differentiate these two conditions. Neurologic and perimetric examinations are often of great help, but even with these aids there are cases in which one remains in doubt as to whether one is dealing with an inflammatory or a noninflammatory swelling.

The more recent advances in physiologic chemistry can be applied to the solution of this problem as well as of some other problems in medicine.

The diagnostic aid that I have to offer is based on the theory that, since in one condition there is inflammatory swelling while in the other there is noninflammatory edema, the protein content of the aqueous should be definitely increased in papillitis while in choked disk it should be within normal limits. This can be expected if one remembers that aqueous is found not only in the anterior and posterior chamber but in the meshwork of the vitreous, and that the circulation of the aqueous

From the Department of Ophthalmology of Rush Medical College, University of Chicago.

is very slow. Products of inflammation can, therefore, reach the anterior chamber by a process of diffusion from the posterior half of the eye.

Partial analyses of the aqueous of the ox were mentioned over one hundred years ago in the writings of Berzelius;[1] analyses of that of man, seventy-three years ago by Kletzinsky.[2] Since then a great deal of work has been done on the subject, and numerous methods of examination have been employed in the study of the aqueous of man and animals. The protein content has been determined by: (1) the refractive index, (2) the viscosity, (3) the surface tension, (4) the precipitation with Esbach's reagent, (5) the nitric acid test and (6) the trichloracetic test, etc.

METHODS

The normal amount of protein in the human aqueous is about 0.02 per cent[3] (as compared with more than 7 per cent in the blood), and the quantity of aqueous available is only from 0.15 to 0.25 cc. (rarely as high as 0.35 cc.). One cannot, therefore, employ the micro-Kjeldahl method of nitrogen determination or some of the other methods which require heavier concentrations of proteins or larger quantities of fluid. Among the reliable methods, and the one used in this work, is the trichloracetic acid test described by Mestrezat and Magitot.[4] It is simple and sufficiently accurate without being too sensitive for clinical use.

The procedure is as follows:

A standard solution of egg albumin containing 1 Gm. of albumin in 1,000 cc. of physiologic solution of sodium chloride is prepared by beating the whites of three eggs to a snow with an equal quantity of 0.8 per cent solution of sodium chloride. This is diluted to five volumes with physiologic solution of sodium chloride and filtered through filter paper. Twenty cubic centimeters of the filtrate is diluted to 400 cc. with the salt solution, and 0.5 Gm. of mercuric cyanide is added as a preservative. From this, dilutions (with physiologic solution of sodium chloride) containing 0.1, 0.2, 0.3 and up to 1 Gm. in each 1,000 cc. are made up in test tubes and used for the tests. These solutions keep for a long time on ice. Eleven hanging drop slides are placed on a glass-topped box painted black on the inside (to facilitate making the readings), and ten of them are marked to correspond to the ten dilutions of egg albumin. One drop of each of the ten dilutions is placed on the concavity of the corresponding slide, and a drop of the aqueous to be tested is placed on the eleventh slide. One drop of 10 per cent (or 20 per cent) tri-

1. Berzelius: Lehrbuch der Chemie, Reutlingen, 1831, vol. 4, p. 442.

2. Kletzinsky, cited by von Jäger, E.: Ueber die Einstellungen des dioptrischen Apparates (Chemische Zusammensetzungen der Augenflüssigkeiten nach Analysen von Kletzinsky), Vienna, L. W. Seidel, 1861.

3. Duke-Elder, W. S.: The Nature of the Intra-Ocular Fluids, Brit. J. Ophth., monogr. supp. 3, 1926-1927.

4. Mestrezat, W., and Magitot, A.: Nature de l'humeur aqueuse de seconde formation chez l'homme et l'animal, Ann. d'ocul. **159**:40 (June) 1922

chloracetic acid is quickly added to each drop on the eleven slides. Each slide is then quickly but gently moved with a rotatory motion on the glass top in order to mix the trichloracetic acid with the albuminous solution. A grayish opacity can now be seen on each hanging drop slide, the degree of turbidity depending on the amount of albumin in each sample. The unknown sample is compared with the various samples as to turbidity, and the slide is placed between the two which it resembles most closely for more careful comparison. If it resembles, for example, the opacity on the slide marked 0.4, the protein content of the aqueous is recorded as 0.4 Gm. per thousand cubic centimeters of aqueous, or 0.04 per cent. The turbidity of the various samples is well enough differentiated against the black background so that one can make the proper readings with comparatively little practice. Daylight is essential for this test, and a black background, such as the glass-topped black box mentioned, makes the readings simple. It is important to have all the drops of equal size. Every piece of apparatus used should, of course, be chemically clean (free from albumin, etc.).

The technic of the anterior chamber puncture is as follows: The eye is anesthetized by instilling one drop of a local anesthetic, such as 0.5 per cent dimethylamino-ethanol hydrochloride, 2 per cent butyn, 2 per cent metycaine or some other preparation, into the conjunctival sac every three minutes until 5 drops have been instilled. The lids are washed with soap and water and then with 1 : 5,000 mercuric oxycyanide. The conjunctival sac is irrigated with the same solution or with some other sterile, nonirritating solution. A self-retaining eye speculum is then introduced to keep the lids separated; the eyeball is fixed with a fixation forceps applied to the conjunctiva near the nasal limbus, and a puncture is made through the clear cornea, 1 mm. from the temporal limbus, with a fine Ziegler knife. A fine hypodermic needle (27 gage) attached to a 1 cc. tuberculin syringe is introduced along the tract made by the Ziegler knife, and the aqueous is carefully aspirated into the syringe; 1 : 3,000 corrosive mercuric chloride ointment is then placed in the conjunctival sac, and a bandage applied. The bandage is removed after twelve hours.

The puncture can be made directly with a sharp hypodermic needle, but as the cornea is very tough the procedure is simplified by the use of the needle knife mentioned. It is better to make the puncture obliquely through the avascular cornea rather than subconjunctivally, as in the latter case blood from the conjunctival vessels may get into the anterior chamber and thus spoil the results. It is well not to empty the anterior chamber completely, as this causes too much capillary dilatation in the iris and ciliary body and even rupture of these vessels, thus increasing the protein content of the aqueous. Puncture of the anterior chamber is free from danger. Injury to the iris can easily be avoided if the point of the needle is held close to the posterior surface of the cornea. Magitot and d'Autrevaux,[5] in 1925, reported 326 anterior chamber punctures without a mishap. As the aqueous which forms after the original aqueous has been removed is very rich in proteins for several hours, at least several days should elapse before a puncture for differential diagnosis is repeated.

REPORT OF CASES

CASE 1.—*Papilledema.*—N. W., a colored man, was admitted to the Cook County Hospital on May 1, 1933, complaining of headache, nausea and vomiting of two

5. Magitot, A., and d'Autrevaux: L'humeur aqueuse en pathologie oculaire, Bull. Soc. d'opht. de Paris, Feb. 21, 1925, p. 395.

weeks' duration. Diplopia as a result of palsy of the left abducens nerve had been present for three weeks. Both disks showed swelling of 3 diopters, and there were numerous hemorrhages on and about the disks. On puncture the spinal fluid was found to be under markedly increased pressure. The palsy cleared up a day after the spinal puncture but recurred. Operation revealed an inoperable tumor of the brain. Suboccipital decompression relieved all the symptoms. The swelling of the nerve heads subsided, and the abducens palsy disappeared. Eight months after decompression the patient was still symptom-free, and the eyegrounds remained normal.

Two-tenths cubic centimeter of aqueous was removed on May 12, 1933. The albumin content was between 0.01 and 0.02 per cent.

CASE 2.—M. D., a white girl, aged 15, was seen at the Cook County Hospital on June 9, 1933, complaining of severe frontal headache, vomiting, diplopia, drowsiness and gradual diminution of vision, of one month's duration. There was palsy of the left abducens nerve. The right disk had an elevation of 4 diopters; the left, of 3 diopters. There were many small hemorrhages and a few yellowish-white degenerative areas in the vicinity of each disk. Urinalysis gave negative results; the blood pressure was normal; the Wassermann reaction of the blood was negative. The peripheral visual fields were normal. The blind spots were enlarged. With a —2.5 sphere in front of each eye, vision was 0.8 in the right eye and 0.6 in the left. The spinal fluid was under definitely increased pressure and clear, and the Pandy reaction was negative. One day after the spinal puncture the palsy disappeared, and the subjective symptoms improved. A neurologic diagnosis of tumor of the posterior fossa was made, and operation advised. The patient refused operation and left the hospital one week after admission.

Aqueous removed from the right anterior chamber on June 9 had an albumin content of 0.02 per cent.

CASE 3.—B. D., a white woman, aged 44, was admitted to the Cook County Hospital on Aug. 10, 1933, complaining of persistent headache, visual disturbance, motor aphasia and intermittent hiccups. In October 1932, a spinal puncture was followed by spastic paralysis of the right arm. In May 1933, she had convulsions. On admission the blood pressure was 128 systolic and 80 diastolic. Roentgen examination, urinalysis and a Wassermann test gave negative results. There was papilledema of 2 diopters on the right and of 3 diopters on the left. Operation, on August 22, disclosed a deep subcortical, solid, inoperable glioma. Decompression was followed by relief from symptoms.

Puncture of the left anterior chamber on August 18 yielded an aqueous with a protein content of 0.02 per cent.

CASE 4.—G. S., a white woman, aged 23, was admitted to the Presbyterian Hospital complaining of severe frontal headache of five months' duration and vomiting for one month. She gave a history of having had infections of the accessory nasal sinuses. There was an abscess of the scalp in the right frontal region. Roentgen examination showed rarefaction of the frontal bone in the region of the right frontal sinus. There was bilateral papilledema of 3 diopters, with marked engorgement of the disks. A few retinal hemorrhages were present in each eye. Spinal puncture on Jan. 9, 1934, showed the fluid to be under a pressure of 22 cm. of spinal fluid and clear. A diagnosis of abscess of the frontal lobe was made, and this was confirmed by operation. Freely flowing pus was evacuated from an abscess in the frontal lobe.

Aqueous removed from the right anterior chamber had a protein content of 0.02 per cent.

CASE 5.—M. M., a white man, aged 45, was seen in the eye dispensary of Rush Medical College in May 1933, with evidence of marked mental deterioration; the history, for that reason, was vague and unreliable. He had 3 diopters of papilledema in the right eye and 1.5 diopters of swelling of the nasal half of the left disk. In addition, there were right homonymous hemianopia and right facial palsy. The neurologic department made a diagnosis of tumor of the left temporal lobe and advised operation. The patient did not return to the clinic. In January 1934, eight months later (in the meantime he had become confined to bed and had lost the power of speech and a left proptosis had developed, he was operated on at the Cook County Hospital, where a very large inoperable tumor of the temporal lobe was found.

Analysis of aqueous in May 1933 showed the protein content in the right eye to be 0.02 per cent.

CASE 6.—M. L., a white woman, aged 34, who was seen in the department of ophthalmology of Rush Medical College in October 1933, had been in an automobile accident eleven months before. At that time she had been unconscious for twelve hours. Her complaints were vertigo, ataxia and occasional loss of consciousness. Vision in the right eye was 0.5; in the left, 0.4. With correction, the vision was 0.8 in each eye. There were 3 diopters of swelling of the right disk and blurring of the nasal margin of the left disk. Both blind spots were enlarged, and the peripheral visual fields for form and colors were within normal limits. Neurologic examination disclosed a paresis of the lower part of the face on the left side. Spinal puncture showed the pressure of the spinal fluid to be 290 mm. of spinal fluid. The fluid was normal. A neurologic diagnosis of multiple traumatic lesions of the brain with atypical epilepsy was made.

The protein content of the aqueous removed from the right eye in October 1933 was between 0.01 and 0.02 per cent.

CASE 7.—V. W., a white man, aged 67, was seen in the department of ophthalmology of Rush Medical College in September 1933, complaining of rapid loss of vision in both eyes for three months and severe left-sided headache, especially in the morning, for two months. Vision in the right eye was 4/200; in the left, 2/200. With correction, vision was 0.2 in the right eye and 0.1 in the left. There was 3 diopters of swelling of each disk. The retinal vessels were markedly sclerosed, and patches of arteriosclerotic retinitis were present in each eye. The right field for form was narrowed to 50 degrees temporally and 30 degrees in the other quadrants, while the red field was constricted to within 10 degrees of the point of fixation. The left field for form was narrowed to 10 degrees, with perception of red present only at the point of fixation. The right blind spot was enlarged; the left fell within the blind field. Six millimeter test objects at 33 cm. were used for the peripheral fields; 6 mm. objects at 1 meter, for the central fields. The systemic blood pressure was 190 systolic and 108 diastolic. The urine contained albumin (2 plus). The medical department made a diagnosis of myocarditis with hypertension. The neurologic findings were negative, and there was no indication for spinal puncture. The protein content of the aqueous was 0.02 per cent.

From these case reports it is seen that in five cases of papilledema in which an increased intracranial pressure was proved by operation (four cases of brain tumor and one of brain abscess) the protein content of the aqueous was 0.02 per cent or less, even though retinal hemorrhages and grayish areas of nerve fiber degeneration were present.

Case 2 was clinically a case of brain tumor, and there was definitely increased intracranial pressure as evidenced by the fact that the spinal fluid was under increased tension and by the relief from all symptoms, including the abducens nerve palsy, following drainage of cerebrospinal fluid. In case 6 there was papilledema due to brain injury. The spinal fluid pressure in this case was 290 mm. Case 7 belongs to the smaller group of cases in which choked disk is caused by conditions other than increased intracranial pressure. In addition to sclerosis of the ophthalmic arteries, as in this case, nephritis, lead poisoning, other intoxications and a few other conditions make up this group. In all of the seven cases of papilledema reported the protein content of the aqueous was 0.02 per cent or less.

Magitot and d'Autrevaux,[5] in reporting the chemical analysis of the aqueous in various pathologic conditions of the eye, found a normal albumin content in papilledema. Chemical analysis of the aqueous in papillitis has not been reported, and as far as could be determined no attempt has been made to differentiate these two conditions by chemical analysis of the aqueous.

Papillitis.—CASE 8.—O. H., a colored man, aged 29, was admitted to the Cook County Hospital in June 1933, complaining of pain, redness of the eyes and blurring of vision for six days. This came on one week after an automobile accident in which the lids of both eyes were injured. Vision in the right eye was 0.1; in the left, 0.2. With the right eye the patient read Jaeger test type no. 1 at 6 inches; with the left, at 11 inches. Roentgen examination showed marked clouding of the maxillary sinuses, but there was no pus on irrigation. Two weeks after admission the redness and pain had subsided, but the vision in the right eye had decreased to counting of fingers at 12 inches. General medical examination, including a Wassermann test of the blood, gave negative results. Slit-lamp examination showed an increased number of cells in the aqueous of both eyes, but no posterior corneal deposits. The irides were normal. Both disks showed an elevation of 2.5 diopters, with some exudates and hemorrhages on and just off the disks. Three weeks after admission the corrected vision was 0.1 in the right eye and 1.5 in the left. The patient left the hospital on a release two days after the refraction. One week before he went home the protein content of the aqueous from the right eye was 0.10 per cent.

CASE 9.—C. B., a colored woman, aged 36, was admitted to the Cook County Hospital in August 1933, with the typical findings of chronic nephritis. There was albumin (4 plus) in the urine; the blood pressure was 208 systolic and 124 diastolic; the blood urea nitrogen was 256 mg. per hundred cubic centimeters (normal, from 8 to 14 mg.), and the creatinine, 14 mg. (normal, 1.4 mg.). The Wassermann and Kahn reactions of the blood were negative. There were bilateral neuroretinitis, with 2 diopters of swelling of each disk, white exudates in the retina and a few retinal hemorrhages. The patient died in September 1933. The protein content of the aqueous was 0.04 per cent.

CASE 10.—B. M., a white woman, aged 18, was seen in the ophthalmologic department of Rush Medical College in October 1933. Five weeks before she had acute rhinitis, more marked on the left. One week later the left eye

became painful, red and tender. The pain was most marked on rotation of the eyes. At the same time the patient noted a large dark spot which occupied the left upper temporal field of vision. For the past week the pain had been present only occasionally. The corrected vision in the right eyes was 1.0 plus 3; in the left, 0.8 plus 3. The patient was able to read the Jaeger test type no. 1 at 10 inches with either eye. On examination there was no redness of the palpebral or bulbar conjunctivae, and no tenderness to pressure. The right pupil reacted normally to direct light; the left, only sluggishly. The consensual reaction to light was normal on the left and decreased on the right. The right disk was normal. The anterior segment of the left eye was normal. The left disk had 3 diopters of dense-appearing, poorly demarcated swelling involving the nasal, superior and inferior portions of the disk. The vessels of the disk were partially covered by swollen nerve tissue and exudate. Several small hemorrhages were seen just below the disk. Examination of the visual fields revealed a positive scotoma occupying almost the entire superior temporal and the upper half of the superior nasal field of the left eye. This scotoma extended from the periphery to within 10 degrees of the point of fixation, was present for form and colors and was continuous with the laterally enlarged blindspot. Medical and neurologic examinations gave negative results. Roentgen examination of the accessory nasal sinuses showed clouding of the left ethmoid sinus. Rhinologic examination revealed impingement of the septum on the middle meatus, apparently interfering with drainage from the middle nasal meatus. Decrease in the swelling of the nerve head and improvement in the visual fields began a few days after submucous resection of the septum and opening of the ethmoid sinus. The protein content of the aqueous from the left eye was 0.04 per cent.

CASE 11.—A. L., a white woman, aged 19, entered the Cook County Hospital in December 1933, complaining of vertigo, headaches, vomiting and weakness for seven months. The blood pressure varied from 198 systolic and 140 diastolic to 215 systolic and 150 diastolic. On one occasion there was albumin (3 plus) in the urine; on another, none. The blood chemistry was normal except for an increase of chlorides to 740 mg. per hundred cubic centimeters (normal, from 540 to 640 mg.). The Wassermann reaction of the blood was negative. The vision was 0.8 in each eye. Both nerve heads showed an elevation of 2 diopters, and there were exudates in the macular regions and a few hemorrhages around the nerve heads. The medical diagnosis was malignant nephrosclerosis.

The protein content of the aqueous was 0.03 per cent.

The protein content of the aqueous in the last four cases varied from 0.03 to 0.10 per cent. It was thus definitely increased above the normal limits. In case 8 there was bilateral papillitis secondary to injury of the orbital tissues. The unusually high protein content was probably due to the great severity of the inflammatory process, as evidenced by the increased cell content of the aqueous. In case 10 there was unilateral optic neuritis secondary to an accessory nasal sinus infection, while cases 9 and 11 were examples of bilateral neuroretinitis of renal origin. In the two cases of papillitis on an inflammatory basis the protein content was 0.04 and 0.10 per cent, respectively, while the protein content of the aqueous in the two cases of albuminuric neuroretinitis was 0.03 and 0.04 per cent.

SUMMARY AND CONCLUSIONS

The determination of the protein content of the aqueous by the trichloracetic acid method is simple and rapid. Aspiration of the aqueous from the anterior chamber is less dangerous than a spinal puncture, does not necessitate hospitalization of the patient and does not impair vision (except during the first hour after the puncture, that is, while new aqueous is being formed; but since the eye is bandaged for a few hours the patient is not aware of this visual disturbance). In this series of cases the albumin content of the aqueous was found to be 0.02 per cent or less, that is, normal, in seven cases of papilledema, while in papillitis of an inflammatory origin it was 0.04 and 0.10 per cent, that is, from two to five times the normal amount. In papillitis of non-inflammatory origin due to transudation of fluid rich in albumin, as in renal retinitis, the protein content was 0.03 and 0.04 per cent, that is, about twice the normal amount, an increase that is also definitely pathologic. The protein determination of the aqueous enables one, therefore, to differentiate choked disk from papillitis. It is realized, of course, that the series of cases presented is small, but the clearcut results obtained and the theoretical soundness of the principles involved warrant the use of this test as an additional diagnostic aid in the differential diagnosis of papilledema and papillitis.

THE FEELING OF UNREALITY

AS A DIFFERENTIAL SYMPTOM OF MILD DEPRESSIONS

JOSEPH C. YASKIN, M.D.
PHILADELPHIA

Feelings of unreality occur in many, if not all, cases of depressive psychosis and are so important in the differential diagnosis that the subject merits special consideration. I have observed this symptom in a series of twenty-eight cases and found it to be a distinct feature in the clinical picture. The patients in all but two of my cases were private patients, and opportunity was therefore afforded for careful and continuous observation. The problems in diagnosis centered largely around differentiation between the psychoneuroses and mild mental depressions. Only two patients required hospitalization, and observations were consequently entirely extramural. This factor, in a measure, probably accounts for the prominence of feelings of unreality, since the degree of depression was never sufficiently severe to mask them. Whenever the feeling of unreality was revealed as a symptom it clearly indicated something graver than a psychoneurosis and pointed the way to a more rational therapy, with better hopes for satisfactory results.

It is recognized, however, that in extramural psychiatric practice it is frequently difficult to distinguish clearly between a psychotic depression and the features of a psychoneurosis. In either case the symptoms are extremely vague and seem to bear no relationship to any specific disorder. The issue of the mental symptoms is often clouded by the varied and numerous somatic complaints that are encountered, and as a natural consequence the question of somatic disease must be considered. When somatic disease is the primary condition, therapeutic efforts should be directed toward the removal or correction of underlying physical causes, and becomes largely a problem for the internist or surgeon. Diagnosis of a psychoneurosis implies that the somatic complaints are, in the majority of cases, merely a coloring of some emotional difficulty, often an unconscious conflict, in which the etiologic diagnosis and treatment depend on well planned psychotherapy. The majority of psychoneurotic persons are best handled as extramural patients, since there are no special precautions or question of hospitalization. Considerable care must be exercised, however, in making an early diagnosis of a psychosis

---

Presented at the meeting of the Philadelphia Psychiatric Society, March 9, 1934.

From the Department of Neurology, University of Pennsylvania, Graduate School.

in the best interests of prognosis and treatment. This is especially true of the mild depressions: first, because of the danger of suicide; second, because these patients are often subjected to futile diagnostic and therapeutic procedures, including mutilating operations, and third, because of the difference in psychotherapy employed.

From my experience, "deep" psychotherapy, often utilized in the management of psychoneuroses, has no place in the treatment of depressions of the manic-depressive type. The method of ventilation and attempts at resolution of unconscious situations, so useful therapeutically in the psychoneuroses, is to be avoided in the depressions as it only causes the patient further unhappiness. In the treatment of these patients judicious encouragement, suggestion and frank discussions should form the psychotherapeutic component of a carefully planned regimen.

The importance of brief attacks of manic-depressive psychosis of the extramural variety was first emphasized by Gregory [1] and was investigated in greater detail in a series of papers by Paskind.[2] These authors emphasized the fact that brief attacks of manic-depressive psychosis are frequently overlooked because the patient's outstanding complaints are somatic rather than mental, because the bulk of the literature on affective psychoses is based on pronounced institutional cases and because the general practitioner is in no position to analyze a complicated and fleeting situation. It is my purpose to stress not so much the brief attacks as the mild and to emphasize the symptom of feelings of unreality which I found useful as a diagnostic criterion.

Important as it may be, the diagnosis of a mild extramural depression is not always simple. A careful history may elicit manic-depressive reactions in other, often distant, members of the family. There may be a history of previous attacks of "stomach trouble" lasting from six to twelve months and successfully treated by diet and medication. The presenting difficulty may be stated to have been precipitated by one or more of the following factors: financial strain, social difficulties, acute infectious disease, childbirth, etc. The spontaneous complaints often lead away from the suspicion of a psychotic reaction. The patient usually stresses the somatic difficulties, such as constipation, abdominal fulness, loss of appetite and weight, insomnia and difficulty in concentration and application. He is convinced that he has trouble in his

1. Gregory, M. S.: Transient Attacks of Manic Depressive Insanity, M. Rec. **88**:1040, 1915.

2. Paskind, H. A.: Brief Attacks of Manic-Depressive Depression, Arch. Neurol. & Psychiat. **22**:123 (July) 1929; Manic-Depressive Psychoses as Seen in Private Practice: Sex Distribution and Age Incidence of First Attacks, ibid. **23**: 152 (Jan.) 1930; Manic-Depressive Psychoses in Private Practice: Length of the Attack and Length of the Interval, ibid. **23**:789 (April) 1930.

stomach, gallbladder or intestines and often has had prolonged treatment for gastro-intestinal or other conditions. Rarely does this type of patient spontaneously complain of being sad, "blue" or "depressed." He regards his nervous symptoms as being produced by somatic disease, and when closely questioned will relate that everything appears changed around him, that things look "unreal," that everything is "foggy." A feeling of unreality has been elicited as a symptom in all cases which on further observation have proved to be true depressions.

A spontaneous complaint of the feeling of unreality is rare, but when patients are asked, "Does everything look or feel natural about you?" they furnish considerable information. Their answers are surprisingly similar in phraseology irrespective of education or native intelligence. Inanimate objects appear "unreal," "foggy," "masked" or "veiled." Most of them say that they see well, that their vision is not impaired. They often add that their immediate relatives and friends have no appeal to them, not because of lack of interest, but because of an "unnatural" feeling. When questioned further they state that they eat, but that all food tastes alike. They all mention a bad taste in the mouth and ascribe it to "bad digestion." Many complain that their entire body feels "unnatural."

The majority of patients affirm that this queer feeling is much more pronounced in the early part of the day, that it tends to be less severe as the day progresses and that it frequently disappears in the evening. With onset of recovery the patient often volunteers the information that the "fog" has lifted.

The feeling of unreality as observed in the depressions is lasting and should be differentiated from the brief, transient attacks of clouding of consciousness observed in toxic, exhaustive and organic states. It should also be distinguished from the various manifestations of anxiety observed in the neuroses and psychoneuroses and from the withdrawal from reality observed in schizophrenia. The feeling of unreality as a lasting, definite symptom has not been observed in the anxiety neuroses or in the psychoneuroses; nor has it been observed in somatic diseases associated with anxiety and depression (Yaskin [3]).

The first patient observed with feelings of unreality was a woman, aged 30, who presented symptoms suggestive of cholecystitis. Later, when somatic disease had been excluded, the condition was diagnosed as a psychoneurosis. She made a complete recovery but had a recurrence five years ago. For the past five years all patients have been questioned as to the existence of this feeling of unreality. The following material is a result of this investigation.

3. Yaskin, J. C.: Nervous Symptoms as Earliest Manifestations of Carcinoma of the Pancreas, J. A. M. A. **96**:1664 (May 16) 1931.

STUDY OF MATERIAL

The material consists of twenty-eight cases; all but two of the patients were private patients, treated extramurally.

Criteria.—The criteria for establishing the diagnosis of mild mental depressions in which the feeling of unreality was a constant symptom were: (1) The absence of definite organic, somatic and metabolic disease as ascertained by careful investigation. Most patients had had complete hospital investigations and some operative procedures prior to coming under observation. (2) An absence of changeability and variability of symptoms and of phobias and compulsions common in the psychoneuroses. (3) The occurrence of some degree of emotional depression, self-accusation and self-derogation at one time or another in the course of the attack. (4) A history of similar previous attacks with long, complete remissions. (5) A history of previous frank manic-depressive reactions. Most of the cases herein reported complied with most of the criteria and each had enough evidence to justify being placed in this category.

Sex Incidence.—There were nineteen female patients (67.9 per cent) and nine male patients (32.1 per cent). This ratio corresponds to the incidence of the frank manic-depressive psychoses as reported by Kraepelin,[4] Bleuler,[5] Strecker and his co-workers,[6] Pollock[7] and others. It differs from the statistics of Paskind,[2] who gives 51.4 per cent for females and 48.6 per cent for males.

Age Incidence.—The ages of the female patients varied from 19 to 55, with an average of 39 years. The ages of the patients in this series are somewhat higher than those reported for hospitalized patients (Kraepelin,[4] Bleuler[5]), the latter probably representing severe types of reactions and those occurring in younger persons.

Hereditary Factors.—A study of the family history of the twenty-eight patients is shown in table 1. Comparing the familial occurrence with those of other observers in table 2, it will be observed that it corresponds grossly to the incidence of psychoses in general, to that of the institutional manic-depressive cases and to that of the extramural group reported by Paskind.

Previous Attacks of Frank Manic-Depressive Reactions.—There were two patients—a man and a woman.

Previous Attacks Resembling Present Attacks.—Fifteen patients (53.6 per cent) gave histories of previous attacks of "stomach trouble" resembling present attacks. Of these eleven (39.3 per cent) were women and 4 (14.3 per cent) were men.

Subsequent development of frank manic-depressive psychoses occurred in two patients—a man and a woman. One remained extramural; the other is still hospitalized.

---

4. Kraepelin, E.: Manic-Depressive Insanity and Paranoia, translated by Mary Barclay, Edinburgh, E. & S. Livingstone, 1921.

5. Bleuler, E.: Textbook of Psychiatry, New York, The Macmillan Company, 1924.

6. Strecker, E. A., and others: Manic-Depressive Psychoses, in Association for Research in Nervous and Mental Diseases, ser. research publ., 1930, vol. 11, p. 471, Baltimore, Williams & Wilkins Company, 1931.

7. Pollock, H. M.: Prevalence of Manic-Depressive Psychoses in Relation to Sex, Age, Environment, Nativity and Race, in Association for Research in Nervous and Mental Diseases, ser. research publ., 1930, vol. 11, p. 655, Baltimore, Williams & Wilkins Company, 1931.

Precipitating causes were obtained in twenty patients. These are summarized in table 3.

Some patients had more than one precipitating cause. In eight no definite precipitating factors could be obtained. These figures compare favorably with statistics of institutional cases reported by Bonner [8] and Travis.[9]

Mode of Onset.—The mode of onset was sudden in four cases (14.3 per cent) and gradual in twenty-four cases (85.7 per cent).

TABLE 1.—*Familial Occurrence in Author's Cases*

Hereditary Neuropathic Factors	Males		Females		Total	
	Number Cases	Per Cent	Number Cases	Per Cent	Number Cases	Per Cent
Direct line (parents)	3	10.7	5	17.9	8	28.6
Indirect (grandparents, uncles, aunts)	2	7.1	8	28.6	10	35.7
Siblings	3	10.7	2	7.1	5	17.8
Total	8	28.5	15	52.6	23	82.1

TABLE 2.—*Comparison with Familial Occurrence in Cases of Other Observers*

	Sane, Koller*	Psychotic Persons in General		Manic-Depressive Psychoses		Depressions Present Series Extramural
		Koller*	Diem†	Institutional, Sumner‡	Extramural, Paskind [2]	
Direct	33	50	57	65.33	67.09	28.6
Indirect	29	12	16	14.76	6.2	35.7
Siblings	5	7	9	4.76	9.1	17.8
Total	67	69	82	85.05	83.2	82.1

* Koller, J.: Arch. f. Psychiat. **27**: 268, 1895.
† Diem, O.: Arch. f. Rassen-u. Gesellsch.-Biol. **2**: 215, 1905.
‡ Sumner, P.: Ztschr. f. d. ges. Neurol. u. Psychiat. **77**: 453, 1922.

TABLE 3.—*Precipitating Causes*

	Female		Male		Total	
	Number Cases	Per Cent	Number Cases	Per Cent	Number Cases	Per Cent
Family discord	7	25.0	2	7.1	9	32.1
Financial difficulties	5	17.9	4	14.3	9	32.1
Surgical operations	3	10.7	..	....	3	10.7
Infections	2	7.1	1	3.6	3	10.7
Childbirth and abortion	4	14.3	..	....	4	14.3
Disappointment in love, etc.	2	7.1	..	....	2	7.1

Duration of Attacks.—The duration of the attacks was determined definitely in eighteen cases. It varied from six weeks to twenty-six months with an average of six and six-tenths months. These figures compare favorably with those of Kraepelin,[4] Bleuler,[5] Strecker [6] and others.

8. Bonner, C. A.: Psychogenic Factors as Causative Agents in Manic-Depressive Psychoses, in Association for Research in Nervous and Mental Diseases, ser. research publ., 1930, vol. 11, p. 121, Baltimore, Williams & Wilkins Company, 1931.

9. Travis, J. H.: Precipitating Factors in Manic-Depressive Psychoses, Psychiatric Quart. **7**:411 (July) 1933.

Analysis of Symptoms.—A bitter taste in the mouth was recorded in twenty-five cases (89.3 per cent), loss of appetite in twenty-two (78.6 per cent), loss of more than 5 per cent in weight in twenty-six (92.9 per cent), pyrosis in nine (32.1 per cent), abdominal discomfort in twenty-six (92.9 per cent), flatulence in ten (35.7 per cent), constipation in twenty-two (78.6 per cent), palpitation in five (17.9 per cent), headaches in seventeen (60.7 per cent), insomnia in twenty-five (89.3 per cent), diffuse numbness in one (3.6 per cent), attacks of anxiety in two (7.1 per cent), emotional depression in sixteen (57.1 per cent), crying spells in eighteen (64.3 per cent), retardation in four (14.3 per cent), suicidal ideas and tendencies in seven (25 per cent) and the feeling of unreality in twenty-eight (100 per cent).

It will be observed that most of these symptoms, considering the high frequency of their occurrence in this series of cases, did not tend to reveal the fundamental nature of the psychotic reactions. The great majority of them occurred in somatic diseases and in the neuroses and psychoneuroses. Even the emotional depression, crying spells and expressed suicidal ideas and tendencies were common in predisposed persons with somatic diseases and in the majority of the neuroses and psychoneuroses. On the other hand, the feeling of unreality was a constant symptom in this series and was not observed in the neuroses and psychoneuroses in which anxiety, conscious or masked, is nearly a constant finding. Nor was the feeling of unreality observed in depressions and anxiety associated with proved somatic disease.[8]

SUMMARY OF ANALYSIS OF MATERIAL

Analysis of sex and age incidence, of hereditary factors, of precipitating causes, of previous similar attacks with complete remissions and of the duration of the attacks studied with complete recovery compares favorably with reported statistics of institutional manic-depressive reactions. The symptomatology, on the other hand, predominantly somatic in character, suggests in these cases the existence of organic visceral disease, serious metabolic disturbance, neuroses or psychoneuroses. Of all the symptoms, the feeling of unreality alone is constant and points away from visceral disease and the neuroses and psychoneuroses in which it was not observed and reveals the psychotic character of the condition. When elicited, therefore, it may be valuable in the presence of many confusing somatic complaints and in the absence of definite psychopathic reactions in disclosing the underlying psychotic process.

PSYCHOPATHOLOGY OF THE FEELING OF UNREALITY

The psychopathology of the feeling of unreality is at present not clear.

The sense of reality, according to Kempf,[10] is a quality attributable to persistence and vividness of the sensations of which objects in the

10. Kempf, E. J.: Psychopathology, St. Louis, C. V. Mosby Company, 1921, p. 66.

environment force one to become conscious when one exposes one's receptors to them. For clinical orientation this definition needs considerable amplification. In the first place, the sense of reality embraces, in addition to the environmental factors, sensations of the body, functions closely related to the vegetative nervous system functions which, true enough, remain unconscious under normal conditions, but which nevertheless exert a definite influence on total reactions. Moreover, reality extends to functions far beyond sensation and perception. It has a definite emotional content, is conditioned by concepts and ideas and is closely related to all psychobiologic activities. Reality, like affect, may be regarded as an integral part of all mentation.

The disturbances of reality may therefore be many and varied, depending on the type and degree of function implicated. Perhaps the simplest form of disturbance of reality is seen in agnosia or imperception in which, as a consequence of definite organic cerebral disease, the patient is able to see, hear, taste and smell objects in his environment but is unable, in spite of extended previous experiences with such objects, to place ideational content in the sensations aroused by them. In agnosia, disturbance of the sense of reality is quantitative and localized, while most other forms of mentation remain normal. In contrast to circumscribed disturbance of the sense of reality observed in agnosia, depersonalization represents a diffuse and extensive form of disturbance. Depersonalization is a disturbance of personality which may manifest itself merely in such mild forms as a feeling of strangeness of the person toward his surroundings and himself. It may attain a degree of severity in which the patient has a loss of self or even a splitting of personality and destruction of the universe. Schilder [11] stated:

> To the depersonalized individual the world appears strange, peculiar, foreign, dreamlike. Objects appear at times strangely diminished in size; at times flat. Sounds appear to come from a distance. The tactile characteristics of objects likewise seem strangely altered. But the patients complain not only of the changes in their perceptivity but their imagery appears to be altered. The patients characterize their imagery as pale, colorless, and some complain that they have altogether lost the power of imagination. The emotions likewise undergo marked alterations. The patients complain that they are capable of experiencing neither pain nor pleasure; love and hate have perished within them. They experience a fundamental change in their personality, and the climax is reached with their complaints that they have become strangers to themselves. It is as though they were dead, lifeless, mere automatons.

Depersonalization is seen in its most marked form in schizophrenia. In this condition the patient believes the morbid symptoms as if they

11. Schilder, P.: Introduction to a Psychoanalytic Psychiatry, translated by Bernard Glueck, Nervous and Mental Disease Monograph ser. no. 50, Washington, D. C., Nervous and Mental Disease Publishing Company, 1928, p. 32.

were real, and acts accordingly. Depersonalization is to be differentiated from withdrawal from reality. "Withdrawal from reality is a withdrawal from contact at higher levels but a return to a phylogenetically older and more diffuse form of contact." [12]

The world of reality is not changed by delusional ideas. "The world of reality . . . has lost its identity, has something separate from him, and is experienced as a sort of concrete interpenetration." [12] Depersonalization has also been observed in hysterical and epileptiform deliria, and here, too, the patient lacks insight. Depersonalization without insight is also observed in depressions. Bleuler [5] stated: "A mild form of depersonalization is comparatively often noticeable in which the patients conceive the outer world as well as their own person as something different and strange." On the other hand, depersonalization may occur as an independent entity and is distinguished as such by reason of the fact that these patients understand the morbid nature of their state, show no disturbance in thought and lead a nearly normal life.[13]

The feeling of unreality observed in the mild extramural depressions appears to resemble in many respects mild forms of depersonalization. These persons realize that their experiences are morbid; that objects in the environment and bodily processes are unchanged; but they experience them as strange, foreign, peculiar, "unreal." As Griesinger [14] stated: "The patient knows what is real, he does not feel it any more. There is a wall between him and things." There can be little doubt that basically the principal disorder is in the affective sphere, although the symptom itself may or may not be a source of annoyance to the patient. In this series it has occurred in the absence of retardation or of appreciable emotional depression and may therefore be of considerable diagnostic aid.

Little can be said regarding the etiology of the symptom. There seems reason to believe that it may occur in states of physical exhaustion and intoxication in which perception and ideation may be organically affected. It may follow emotional shock, when it may be wholly explained or partly explained on a physiologic basis via the endocrine and vegetative nervous system. None of my patients was psychoanalyzed, but depersonalization as a syndrome is traceable from the

12. White, W. A.: Essays in Psychopathology, Nervous and Mental Disease Monograph ser. no. 43, Washington, D. C., Nervous and Mental Disease Publishing Company, 1925, p. 53.

13. Morgenstern, S.: Psychoanalytic Conception of Depersonalization, J. Nerv. & Ment. Dis. **73**:164 (Feb.) 1931.

14. Griesinger, quoted by Morgenstern.[13]

psychoanalytic standpoint to unsuccessful sublimation, to a renunciation of sexual pleasure or to a fright suffered in childhood.[15]

SUMMARY

The diagnosis of mild extramural depressions is often difficult because of absence of clear psychotic symptoms and the prevalence of numerous somatic complaints which suggest the existence of somatic and metabolic diseases or of neuroses and psychoneuroses.

In these cases the "feeling of unreality" was a constant symptom in a series of twenty-eight cases and it was not elicited in somatic disease or in the neuroses and psychoneuroses. This symptom may therefore be useful for differential diagnosis in doubtful cases.

The feeling of unreality is probably a mild form of depersonalization in which the patient is aware of his abnormal reactions to his environment and his own somatic and mental processes.

ABSTRACT OF DISCUSSION

DR. K. E. APPEL: I am grateful to Dr. Yaskin for pointing out a symptom that has probably been overlooked, and for calling attention to an aid in distinguishing psychoses from psychoneuroses. I think that Dr. Yaskin makes out a good case for a group of cases that are often overlooked or perhaps wrongly diagnosed. I certainly shall be on the lookout more than ever for the symptom that he describes.

In thinking over cases in which I recall having observed this symptom, it did not seem to occur in depressions so universally as in Dr. Yaskin's series. My memory was that I found feelings of unreality in patient's with psychasthenia, hysteria and mild schizophrenia. I went to my notes and looked up those that I could find relevant to these points, and it seemed to me that a feeling of unreality occurred more frequently in these conditions than in cases of mild depressions. There were patients who did not have self-accusation or remorse, but there were feelings of futility and inadequacy. I did have, of course, some cases that presented the symptoms described by Dr. Yaskin.

I was interested in the psychopathology of which Dr. Yaskin spoke. First he mentioned an organic condition in which is found the condition of unreality. I recall reading Dr. Harris' article on hypoglycemia, a condition in which one often finds this symptom. A physician in conversation told me that he had observed a number of cases of hyperparathyroidism that had been diagnosed as presenting neurotic symptoms. In exhaustive states this symptom of unreality exists. A student who had been studying much late at night and became exhausted gave this as his chief complaint. A girl had severe pyelitis following pregnancy, which necessitated an operation and several transfusions. Following this there was a feeling of unreality as well as the fear that she would lose her mind. There were no signs of depression that I could find. In cases of psychasthenic fears patients have had such a feeling of unreality. The psychologic basis of that, so far as I was able to tell, was a defense against savage impulses. In mild depressions in which I have seen this symptom it seems that there could be discovered feelings of marked antagonism and resentment toward some persons in the immediate environment. The instinctive feelings of aggression directed against these people

15. Nunberg, M.: Depersonalization im Lichte der Libido-Theorie, Internat. Ztschr. f. Psychoanal. **10**:1, 1924. Federn, P.: Narzissmus im Ichgefüge, ibid. **13**:420, 1927.

became directed against the patient himself. As to depersonalization, when there is a more minute dissociation of the personality into small discrete elements, whether in schizophrenia, hysteria or sometimes in depression, I thought that I could discover marked feelings of guilt, in which one force of the personality seemed to be trying to control impulses in the other side of the personality which were taboo, but for which the patient felt the need of punishment. It seems to me that the depersonalization phenomenon is one which in my experience has been related to the problem of guilt and the working out of that problem in the personality.

I wish to ask one question. Did Dr. Yaskin state that in 58 per cent of cases he found depressive symptoms? If so, in the other cases what did he think was the basis of the diagnosis of a manic-depressive condition?

DR. S. F. GILPIN: I agree with Dr. Yaskin as to the difficulty in differential diagnosis between mild depressions and the psychoneuroses. The feeling of unreality may not be pathognomonic of mild depression, but I have yet to see it in a psychoneurosis. The mildly depressed patient is very apt to complain in just this way, especially in depressions occurring among educated people who are well able to think about themselves, to read books and to study their own cases. I have under care now a physician with a mild depression which has lasted one and one-half years. It is not so severe as to interfere with his work, with the exception of one month's rest a year ago. It is interesting to hear him try to describe his feelings. "I do not know what this is, but there is something that seems to come down on my head and things do not seem right to me." "I felt this morning I must jump off the bridge, but I feel better after talking to you and I can now see my patients." Another patient, a clergyman, was told he had neurasthenia. Finally, after reading a book on depression he was convinced that that was the proper diagnosis in his case. His expression many times was, "Doctor, things seem so unreal to me." It was natural that the first diagnosis was neurasthenia, as all of these depressions begin with symptoms of exhaustion.

The point has been made as to a precipitating cause. I do not believe that there is a precipitating cause without the patient. I have seen depression develop when there was every reason externally for the patient to be happy and contented. I have seen the same patients remain happy and in good health mentally when there was every outside influence to precipitate an attack.

I was interested in the remarks about hypoglycemia and hyperparathyroidism. If one knew enough about the etiology of these conditions one might find that something of this order is the cause of the periodic depressions as well as of the opposite extremes, the periodic exaltations.

DR. BARON: Dr. Yaskin's restrictions of a feeling of unreality as a differential symptom of mild depressions is unwarranted by clinical psychopathologic studies. One not infrequently gets this expression as a sign of psychic regression and splitting of the personality. I wish to ask Dr. Yaskin whether he correlated the morphologic observations made on his patients with his so-called differential sign?

DR. C. A. PATTEN: I had the privilege of reading Dr. Yaskin's paper this week and not until reading it had the idea occurred to me to look for this symptom as a sign of mild manic-depressive psychosis. I confess that there is a question in my mind as to just what is the definition of the phrase "unreality feeling." What is reality and what is unreality feeling? If Dr. Yaskin's cases have shown this so strikingly and the final diagnosis has turned out to be mild manic-depressive reaction, it should be an easy matter to elicit it in practice. I have a suspicion that the symptom of unreality may appear in many conditions, but I presume Dr. Yaskin means a sense of unreality extending over a long time.

DR. JOSEPH YASKIN: In reply to Dr. Baron, I may state that no morphologic observations were made in the study of the cases.

Regarding Dr. Appel's and Dr. Patten's discussion, a great many topics require further elucidation. The feeling of unreality, as I observed it, consists of spontaneous complaints or, more frequently, complaints on questioning that everything about and within the patient appears strange. While it was a fairly constant

symptom in the cases studied, it was not painful and should in the first place be differentiated from anxiety, which is the prominent symptom in the various psychoneuroses to which Dr. Appel referred. It is true that in the psychoneuroses, and especially in some of the anxiety states, the patient often complains that she is different, that something terrible is going to happen to her, but it is my belief that this syndrome is vastly different from the feeling of unreality to which I have referred. The feeling of unreality is not an anxiety manifestation. At the same time, I do not wish to be understood that the feeling of unreality may not occur in neuroses as a brief, transient phenomenon; it undoubtedly occurs in some of the psychoses other than depressions.

The feeling of unreality that was reported in hypoglycemia and other organic states was probably not of the same character as that reported here; it is likely a disturbance of perception closely allied to agnosia.

Dr. Gilpin's remarks are interesting and practical. I agree with him that in studying cases of this sort a careful history is extremely important. I have stressed, in the paper, that previous attacks may have been regarded and treated as somatic disease or some form of neurosis, the depressive elements having been entirely or nearly entirely disregarded. In this connection the criteria that were laid down in the body of the paper are useful in helping to establish a diagnosis.

Clinical Notes

TUBEROUS SCLEROSIS WITH UNUSUAL LESIONS OF THE BONES

JACQUES S. GOTTLIEB, M.D., AND GEORGE R. LAVINE, M.D., WORCESTER, MASS.

Cases of tuberous sclerosis (epiloia), a rare form of cerebral sclerosis, have appeared so infrequently in the literature that new cases warrant reporting. Probably the earliest description of a case, by von Recklinghausen in 1863,[1] was that of a newly born child who showed sclerotic areas in the brain and myomas in the heart muscle. Bourneville [2] recognized the condition as a pathologic entity, and from the potato-like shape of the sclerotic patches in the brain originated the name tuberous sclerosis. In spite of many pathologic descriptions this condition was not recognized clinically until 1908, when Vogt [3] described the syndrome as characterized by the triad of adenoma sebaceum, convulsive seizures and mental deficiency. Since then there have been several series of case reports by Sherlock [4] (nine cases), Lind [5] (eight cases), Brushfield and Wyatt [6] (sixteen cases), Yakovlev and Guthrie [7] (four cases) and Critchley and Earl [8] (twenty-nine cases).

Throughout these reports one is struck by the protean nature of the disease in its possible involvement of any of the systems of the body. Not only can there be absence of any one member of the characteristic triad, but in conjunction with any combination there has been confirmed the presence of neoplasms of any or all of such organs as the kidneys, heart, spleen, lungs and retina. Associated with these various findings, numerous forms of so-called degenerative stigmas have been described, thus tending to create innumerable variations in the clinical picture. The present case, although conforming in general to the fundamental symptomatology, has several unusual findings which warrant its description here.

From the Psychiatric and Medical Services of the Worcester State Hospital.

Presented before the Boston Society of Psychiatry and Neurology, April 26, 1934.

1. von Recklinghausen: Verhandl. Berl. Gesellsch. f. Gebürtshülfe **15**:75, 1863.

2. Bourneville: Scléreuse tubéreuse des circonvolutions cérébrales; idiotie et épilepsie hémiplégique, Arch. de neurol. **81**:1, 1880.

3. Vogt, H.: Zur Pathologie und pathologischer Anatomie der verschiedenen Idiotie Formen: II. Tuberöse Sklerose, Monatschr. f. Psychiat. u. Neurol. **24**: 106, 1908.

4. Sherlock, E. B.: The Feeble-Minded, New York, The Macmillan Company, 1911.

5. Lind, W. A. T.: Epiloia, M. J. Australia **2**:290, 1924.

6. Brushfield, T., and Wyatt, W.: Epiloia, Brit. J. Child. Dis. **23**:178 and 254, 1926.

7. Yakovlev, P. I., and Guthrie, R. R.: Congenital Ectodermoses in Epileptic Patients, Arch. Neurol. & Psychiat. **26**:1145 (Dec.) 1931.

8. Critchley, M., and Earl, C. J. C.: Tuberose Sclerosis and Allied Conditions, Brain **55**:311, 1932.

REPORT OF A CASE

History.—B. K., a white woman, aged 23, was admitted to the Worcester State Hospital on July 21, 1927, the commitment papers stating that she was incoherent in speech and irresponsible in action. She had become so noisy and destructive that it was impossible to care adequately for her at home.

Both maternal and paternal grandparents were born in Germany, were of good intellect and prosperous, and had lived past the age of 70. The parents were in good health, the father being a draftsman and engineer. The siblings, of whom there were three, all older than the patient, were intelligent and in good health. Of two brothers, one had been graduated from high school and the other from college. A sister was a graduate nurse. There was no history of any hereditary disease or degenerative stigma in the family.

The patient was born in a large city in Massachusetts on Nov. 27, 1909. The mother was in good health during the pregnancy, but labor was much more prolonged than in her previous three deliveries. The weight at birth was 9 pounds (4.1 Kg.). At birth a large reddish-brown patch with multiple elevated areas was noted on the right side of the neck. At about the age of 6 months, when the patient first began to sit up, it was observed that she held her head almost continually to the right. This was not recognized as an abnormality until the child was 11 months old. Attempts to walk began at 1½ years of age, but success was not attained until she was 3½. She was never able to say more than a few intelligible words, and her conversation consisted chiefly of inarticulate grunts.

At the age of 3 she began to have convulsive attacks during which she would become rigid, fall, and have tonic and clonic spasms which would persist for about four or five minutes. These attacks began suddenly, and during the first year of their appearance occurred about once a week. As she grew older they became less frequent, so that after seven years they had completely disappeared.

During this time the reddish-brown patch noted at birth increased in size. In addition, "raised white patches" on the face and back and "reddened nodules" over the face appeared and gradually increased in size and number. These are described under the report on the skin.

The patient grew very rapidly until she was larger than any of the other children. The larger she became the more clumsy and awkward were her movements. There were many peculiar motions of the hands, which were continually active in picking and fumbling at her clothes, and a coarse tremor was evident when she attempted to pick up objects. She did not learn to dress herself or to perform any complicated act. Partly because of awkwardness and inability to talk, she never played with other children. Her interest was difficult to arouse, and her favorite amusements consisted in either banging a tin can with her hand, attempting to make as much noise as possible, or sitting in a rocking chair for hours, grunting loudly as she rocked. She was described as frequently laughing and smiling in a "silly, idiotic" fashion.

Efforts to teach her various things met with little success. Counting was never learned. The mother considered the inability to speak of fundamental importance, but felt that the child could understand simple instructions. It became more and more difficult to care for her, since destructiveness was added to her noisiness. If not allowed to have her own way she became angry, and would throw any handy objects at people near her. Because of this behavior and her physical strength and size, all members of the family lived in fear of being injured. As her violence and destructiveness increased, and as she was untidy and incontinent, it became impossible for the parents to care adequately for her at home. She was therefore committed to this hospital.

Mental Symptoms.—Throughout the patient's stay of seven years in the hospital her behavior has remained about the same. She is an awkward, but well developed and nourished white woman who immediately attracts attention because of the papular eruption over the face. As she sits docilely in the ward, her head usually hangs forward, her eyes wander aimlessly about, and the facial expression which she maintains is dull and vacant. Occasionally there is a ticlike movement of the right side of the face, involving mainly the mouth. Her smiles, which come and go, are of the silly and idiotic type. It is only by constant attention that her appearance is kept fairly neat, for she is untidy and incontinent.

She appears to be totally indifferent to activities in the ward and people, makes no attempts at contact, and usually wanders away from the other patients, desiring to sit alone. On the other hand, she is easily led and follows trotting at one's heels with an awkward, peculiar, right-sided, loping gait.

Toward anything strange or new she usually becomes resistive and uncooperative. At other times she is noisy, grunting and squawking loudly. On rare occasions she is destructive, pushing benches around, destroying paint on the walls or breaking window panes. These irritable periods, however, are of short duration.

Her speech is limited almost entirely to unintelligible grunts, yet she seems to understand simple statements, for she is able to reply by nodding her head correctly. There is difficulty in conversation, since besides her language handicap she demonstrates marked distractibility, as noted by sudden shifts in attention. No hallucinations or delusions can, under the circumstances, be elicited. Her orientation, memory and judgment are extremely limited.

Three psychometrists derived independently, at different times, the following results: Kuhlman-Stanford mental age, 2 years, 6 months; intelligence quotient, 18 (14 year basis). Tests with the Gesell preschool schedule showed a marked consistency with these results and pointed to a rating of about 2 or 2½ years. The results were considered fairly representative, but because of her distractibility and inability to talk, and the fact that these tests are standardized on infants, they were not considered reliable. The general behavior of the patient corroborates these results and points with some certainty to an idiot's level of intelligence.

Physical Examination.—The patient was well developed and nourished, was 5 feet and 7 inches (170.18 cm.) tall and weighed 138 pounds (62.6 Kg.).

Skin: There were numerous well developed lesions scattered over the entire body. On the face (fig. 1) was typical adenoma sebaceum, which consisted of a nodular reddish rash distributed in a "butterfly-shaped" area over the nose and cheeks. The numerous papules, which blanched on pressure, were firm and projected above the skin from 1 to 5 mm. The larger ones were near the nose, particularly in the nasolabial folds. Although the chin was finely stippled with very small papules, the absence of any on the lips presented a striking circumoral pallor. On the right side of the neck was a large, deep reddish-brown, pigmented, coarsely granular area, slightly irregular in outline, measuring 6 by 4 cm. and containing numerous large papillomas. On the forehead were two elevated areas, one on the right above, and the other on, the supra-orbital ridges. The one on the right measured 3 by 1.8 cm.; the one on the left, 2 by 1.5 cm. They were soft and compressible and felt as though they were composed of a gelatinous material. Their color was that of the surrounding skin. Posteriorly, over the lower thoracic region of the spine, was a typical so-called "shagreen patch" measuring approximately 9 by 4.5 cm. It was flesh-colored, slightly raised and irregularly shaped, and had an uneven thickening of the skin. Its distinguishing characteristics were marked softness and an extreme dilatation of the sebaceous

ducts from which projected very fine lanugo hairs. Over the extremities were scattered numerous small, flattened, brownish, pigmented areas, about 1 to 2 mm. in diameter. There was one small brownish pigmented nevus in the left sacro-iliac region.

Biopsy: A piece of skin containing numerous papillomas was removed. Microscopic examination revealed the skin surface thrown into many irregular-shaped papillary projections, under which there was a large cystic cavity lined by a thin strip of normal-appearing epidermis. This cavity was filled with coarse, granular, basic-staining material. In addition, in the dermal layers were numerous groups of normal-appearing glandular acini made up of large, irregular vesicular, circular cells with a centrally placed, relatively small nucleus and with the cytoplasm organized into a fine mesh network. These acini were entirely encapsulated by a thin strip of connective tissue. The nuclei presented no variation as to size, shape and staining reaction. No mitotic figures were found. Throughout the dermal layer many small vessels had thickened collars lined by cuboidal endothelium with a dense connective tissue wall. These were prominent throughout the section. There was a marked increase of dense, connective tissue stroma throughout the entire dermal layer. The diagnosis made was: papillomas, adenomas of sebaceous glands, and chronic periarteritis with fibrosis, resulting in obliterative endarteritis.

Eyes: External examination gave negative results. The ophthalmoscope revealed flat retinal tumors or "phakomata." In the right fundus was a large, oval, hazily outlined, grayish area, slightly elevated, about half the size of the optic disk, located to the nasal side, just below the position of 3 o'clock (fig. 2). At the periphery of this tumor were numerous fine capillaries, interwoven into a fine mesh, which dipped into the tumor substance. There appeared to be a small artery running from the disk to the tumor itself. No inflammatory reaction was noted. In the left fundus were two similar areas, but only about half the size of the one on the right, located at about 3 and 11 o'clock. These did not appear to be in any close relationship with blood vessels. In both fundi the optic disks and retinal vessels appeared normal. The visual fields could not be determined because of lack of cooperation.

Developmental Abnormalities: The ears were excessively large, but fairly well shaped. The left had a large, firm, flesh-colored fibroma, 6 mm. in diameter, on the tragus. The hard palate was highly arched and narrow. The tongue was long and slender. The hands were of the simian type. There was flattening of thenar and hypothenar eminences. There was incurving of the little fingers. Roentgenograms of the sacrum revealed a spina bifida. Thorough physical examination of the various systems of the body did not reveal any abnormalities except those already stated.

Neurologic Examination: This was conspicuous because of the paucity of positive findings. The cranial nerves, as far as could be determined, revealed no abnormalities. The motor system presented the following minor anomalies: The arms were extremely weak and, possibly owing to the lack of development of the hands, the patient was unable to grasp well. On attempted movements there was a marked intention tremor of the right arm. There was a definite diminution in the muscular tone of the arms and hands. Undue mobility was present at all joints. No definite atrophy or involuntary movements were noted. Coordination tests could not be performed. Sensory examination could not be made owing to the poor cooperation of the patient. The reaction to gross stimuli was such, however, that cutaneous sensation appeared to be approximately normal.

There was a generalized hyperreflexia involving the biceps, triceps, radial periosteal and ankle and knee reflexes, but these reflexes were of equal strength on the two sides of the body. There were no abnormal reflexes. The pilomotor reflex was conspicuously active.

Laboratory Examination.—Blood morphology: Examination of the blood showed: hemoglobin, 70 per cent; red cells, 3,700,000; white cells, 8,650; polymorphonuclears, 66 per cent; lymphocytes, 25; eosinophils, 5; transitionals, 4, and basophils, 0.

Blood chemistry showed: nonprotein nitrogen, 30 mg. per hundred cubic centimeters; urea, 17 mg.; uric acid, 2.87 mg.; creatinine, 1.34 mg.; sugar, 95 mg.; cholesterol, 148 mg.; calcium, 9.8 mg.; phosphorus, 3.5 mg.; whole blood (carbon dioxide) 55.16 volumes per cent; carbon dioxide-combining power, 65.96 volumes per cent; p_H, 7.41. The Wassermann reaction of the blood serum was negative.

Urine: Samples gave negative results for sugar, albumin and acetone. Microscopically, the constituents were normal. A Mosenthal test revealed no fixation

Fig. 1.—Lateral view of the patient showing the distribution of adenoma sebaceum, pigmented area on the neck, soft, raised, flesh-colored area over the right eye and the large normal shaped ear.

of specific gravity or increased output of urine at night. The Bence-Jones protein reaction was negative.

Dextrose Tolerance Test: Ingestion of 100 Gm. of dextrose resulted in the following blood sugar readings at half-hour intervals, after a fasting level of 93 mg. per hundred cubic centimeters: 159, 169 and 109. Sugar in the urine for the four half-hour periods was 52, 41, 73 and 52 mg. per hundred cubic centimeters.

Lumbar Puncture: The initial pressure was 140 mm., with good pulsations present. The fluid was clear. There was a rapid rise and fall on jugular and abdominal pressures. Final pressure after removal of 12 cc. of fluid was 80 mm. Examination of the fluid revealed: lymphocyte, 1; globulin, 0; sugar, 98 mg.; protein, 22 mg.; chloride, 0.718 mg.; colloidal gold curve, 0000000; Wassermann reaction, negative.

Electric Reactions of Muscles: All the muscles of the hands showed normal response to faradic and galvanic currents.

Basal Metabolic Rate: The rate was normal—106 by the Harris-Benedict and 101 by the DuBois standards.

Electrocardiogram: In lead I there was a low Q R S complex and the height of the T_1 wave was only fair. Lead II showed notching of the Q R S and the T_2 wave was high. Lead III was low throughout. The heart rate was 70. This pointed to some evidence of an interference with the conductive mechanism of the heart.

Roentgenograms: Roentgenograms of the abdomen revealed spina bifida of the sacrum with no other abnormal findings. Flat plates of the kidneys showed no abnormality. Those of the cranium showed a peculiar mottling, with indistinct islands of increased density alternating with areas of rarefaction throughout the bone. Both the internal and the external tables appeared thicker and denser than

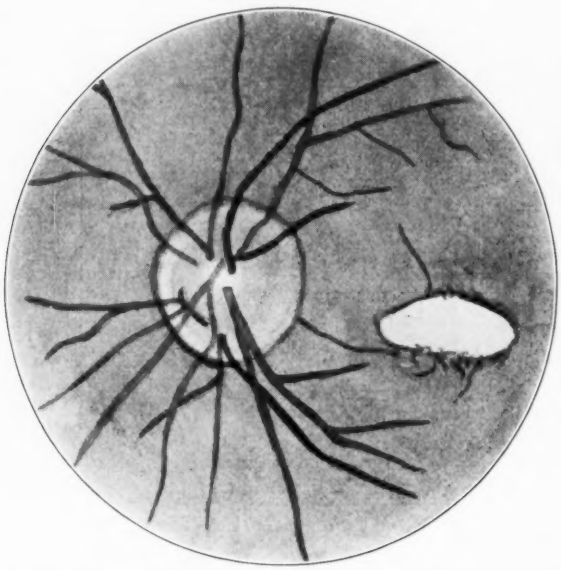


Fig. 2.—Drawing showing the right fundus containing the retinal tumor and its association with blood vessels.

normal. There were no areas of destruction visible or general signs of increased pressure. The sella was normal (fig. 3).

Pictures of the hands and feet revealed periosteal thickening and generalized osteoporosis of both metatarsal and metacarpal bones and their associated phalanges. There was also a generalized fragmentation of the cortical layers. Several of the bones of the hands showed areas of marked rarefaction, a few millimeters in diameter, suggesting small cysts (fig. 4). Yet there were no abnormalities seen in any of the long bones, spine or ribs. Neither were there any enamel or dental abnormalities.

COMMENT

This case presents many of the typical findings consistent with the diagnosis of tuberous sclerosis. The cutaneous lesions, as verified by the typical observations at biopsy, the marked mental deficiency and the history of epileptic attacks are the

triad on which the diagnosis depends. The unusual findings in this case are limited to the retinal tumor of the right fundus and the lesions of the bones.

Van der Hoeve, in 1923,[9] was the first to report flat tumors of the retina. Although their occurrence is rare even in this disease, they have always been reported as showing no relationship with retinal blood vessels.[10] In this case, however, the tumor of the right fundus was surrounded by numerous fine capillaries which dipped into its substance. Moreover, there was a distinct vessel coming from the optic disk to the tumor itself. This tumor, therefore, seems to be midway between the one described in Hippel-Lindau's disease, in which there are numerous associations of blood vessels with the retinal tumor, and the one without vessels found in tuberous sclerosis. This is some evidence to confirm van der

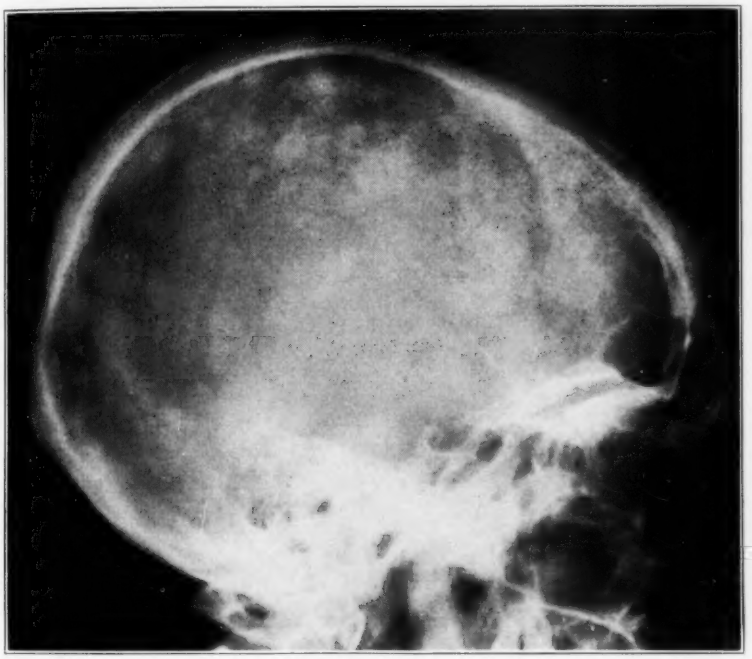


Fig. 3.—Roentgenograms showing the indistinct islands of increased density alternating with areas of rarefaction throughout the bone and the thicker and denser tables of the skull.

Hoeve's contention that Hippel-Lindau's disease and tuberous sclerosis are closely associated or are different manifestations of the same disorder.

The lesions of the bones present puzzling pictures as revealed by roentgenograms, and they are difficult to interpret. Van der Hoeve[9] reported that Pincherle and Horniker found "osteoporosis and pneumatization of the bones of the skull and

9. van der Hoeve, J.: Eye Diseases in Tuberose Sclerosis of the Brain and in Recklinghausen's Disease, Tr. Ophth. Soc. U. Kingdom **43**:534, 1923.

10. van der Hoeve, J.: Eye Symptoms in Phakomatoses, Tr. Ophth. Soc. U. Kingdom **52**:380, 1932.

typical vascular enlargements in the vessels of the diploe." Van Wulfften Palthe implied that one of the tumefactions might affect the parathyroid gland, thus causing the appearance of osteitis fibrosa cystica. Paget's disease, localized tumors, and cysts have also been reported. Thus, for consideration of the differential diagnosis of the lesions of the bones in this case the following conditions have been considered: hyperparathyroidism, multiple myeloma, osteoplastic sarcoma and a neurotrophic or chronic inflammatory lesion.

A diagnosis of hyperparathyroidism cannot be substantiated in view of the limited lesions of the bones and the repeated findings of normal blood serum calcium and phosphorus associated with normal blood nonprotein nitrogen and uric

Fig. 4.—Roentgenograms showing periosteal thickening, osteoporosis and cystic degeneration.

acid. Even though tumors of the parathyroid glands have been found post mortem without any of the characteristic changes in the blood a diagnosis cannot be made based on the roentgen findings alone. Multiple myeloma seems ruled out by the normal appearance of most of the bones and the negative Bence-Jones albuminose test in the urine for without pathologic confirmation it is impossible to do more than hint at such a diagnosis. An osteoplastic sarcoma must be considered in view of the areas of rarefaction of osteoid material in the skull that are suggestive of metastases. Yet, absence of any discernible primary lesion and the inconsistency of the appearances of the roentgenograms of the extremities again make it impos-

sible to suggest this as a reasonable cause. Moreover, the lesions being limited to the skull and extremities seemingly must be associated, and therefore implicate a generalized disturbance involving the calcium metabolism.

By exclusion, therefore, one must consider a neurotrophic disturbance causing these changes of the bones, possibly as a result of the "tuberous" lesions of the brain. Furthermore, it is possible that these lesions are the result of chronic inflammatory processes. Either explanation is unsatisfactory, and for diagnosis biopsy of the abnormalities of the bones and studies of the calcium metabolism are required.

SUMMARY

A case of tuberous sclerosis, characterized by typical adenoma sebaceum, mental deficiency, a history of convulsive seizures and developmental stigmas, is presented. The unusual features are: (1) a retinal tumor of the right fundus which has fine capillaries dipping into its substance and a definite vessel running from the optic disk to the tumor itself, and (2) peculiar bony lesions limited to the skull and extremities, characterized by osteoporosis, mottling in the skull, periosteal thickening and destruction of the cortical architecture. The metacarpal bones and their associated phalanges show a few round areas of increased rarefaction suggesting cysts.

DISCUSSION

Dr. Paul I. Yakovlev: Tuberous sclerosis is rare. However, because of the frequency of the association with epilepsy, it is to be expected that in an institution for epileptic patients one would see more such cases than in other institutions. We have several cases of tuberous sclerosis at Monson. The cutaneous anomalies characteristic of tuberous sclerosis are often associated with other congenital anomalies, among which Recklinghausen's neurofibromatosis and angiomatosis are particularly frequent. It is noteworthy that the distribution of the anomalies of the skin is steadily maintained in most of the typical cases, the integument of the face and sacrolumbar region being affected with definite predilection as compared with the other regions. The same feature, while less prominent, is manifested also in the distribution of the cutaneous anomalies in angiomatosis and in neurofibromatosis. All these congenital anomalies are exceptional in distal regions of the body, e. g., the hands and feet. They occur more frequently near the midline of the body, being always more common on the dorsal aspect of the trunk than on the ventral, and being especially frequent in the cephalic and caudal segments. According to the prevalence of the three varieties of congenital anomalies of the integument, there may be observed all degrees of transition from a typical case of tuberous sclerosis to one of either pure neurofibromatosis or of angiomatosis. The case presented by Drs. Gottlieb and Lavine illustrates the association of these other varieties of congenital anomalies with those of tuberous sclerosis. Indeed, their patient presents, apart from skin lesions most characteristic of tuberous sclerosis on the face and in the lower dorsal region, pedunculated neurofibromas in the intergluteal folds, "café au lait" nevi and pigmented nevi. Moreover, the lesion on the face reveals an excessive proliferation of small blood vessels and capillaries enmeshed in connective tissue fibers. One often sees this in a typical trigeminal angiomatosis of the face. There are arguments in support of the view that in the background of all these congenital anomalies of the skin there exists an embryonal disturbance of the differentiation of ectodermal elements, the eventual prevalence of mesodermal elements (blood vessels and connective tissue) in their structure being a secondary process. In view of all these considerations, in part speculative, I wish to suggest that the unusual bony changes revealed in the present

case are a part of the general picture of congenital abnormalities in the differentiation of tissues of ectodermal derivation. Indeed, there exists a form of cystic Recklinghausen's disease of the bone which develops from the periosteal schwannomas, leading eventually to a process in the bone itself not unlike that of rarifying osteitis of Paget, with the formation of cystic cavities in the bone. In other words, one deals originally with periosteal schwannoma, homologous to the schwannoma of the skin, peripheral nerves, stomach, intestines, appendix and other organs provided with nerve fibers. This seems a plausible interpretation of the unusual changes in the bones revealed in the present case of tuberous sclerosis. The observation of Drs. Gottlieb and Lavine is extremely valuable and roentgen examinations should be made in other cases of this condition.

TRIGEMINAL NEURALGIA: A NEW INSTRUMENT FOR ALCOHOLIC INJECTIONS

WILLIAM J. VAN DEN BERG, SACRAMENTO, CALIF.

Alcoholic injection into the second and third divisions of the trigeminal nerve is a common procedure in all neurosurgical clinics. The success of the procedure and the duration of the relief from pain are entirely dependent on the injection of the alcohol within the nerve itself. The operator is most skilful who can insert the point of the needle within the nerve on the first attempt, without numerous withdrawals and repeated attempts, changing the direction of the needle each time.

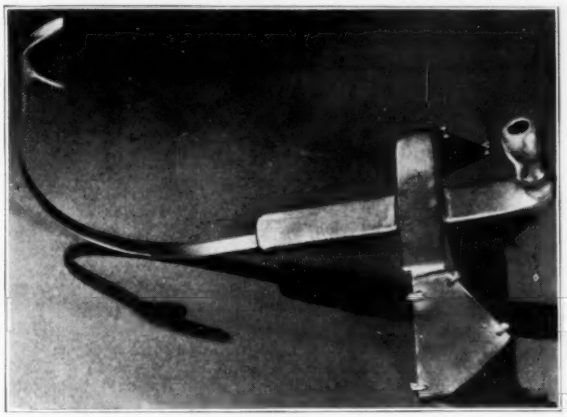


Fig. 1.—Instrument for alcoholic injections into the second and third divisions of the trigeminal nerve.

It was because of the high percentage of failure of the older method in locating the various landmarks and trying to determine the proper angle by sight that Grant [1] originated a more precise method with the aid of a zygometer and a protractor, by the use of which the successful primary results of the alcoholic injections were greatly increased.

After considerable study and dissecting I thought that the improved technic of Grant could be simplified and yet assure as great a success. As a result, the instrument shown here (fig. 1) was designed. The angles of the guides were determined after numerous dissections of the second and third branches of the trigeminal nerve. Further check-ups on the cadaver after completion of the instrument and the results obtained with alcoholic injections in living patients have proved the success of the instrument. Of ten injections of alcohol performed over varying periods during fifteen months, all have afforded complete relief up to the present time, except in one patient, in whom the injection had to be repeated

1. Grant, F. C.: Anatomic Study of Injection of Second and Third Divisions of Trigeminal Nerve, J. A. M. A. **78**:794 (March 18) 1922.

within three months of the first owing to regeneration of the nerve, signifying that the alcohol in this case had not been injected into the center of the nerve.

The instrument consists of a flat bar which fits against the zygomatic arch. At the anterior end of the bar is attached a curved spring, because of which the instrument will fit an adult head of any size. At the posterior end of the instrument is attached a button which fits into the external auditory meatus, and at the anterior end a V shaped piece of metal is attached which fits over the root of the nose (fig. 2). The guides, which are grooved for the passage of the needle, are attached to the part of the instrument placed against the zygomatic arch.

The instrument is reversible, and can be used on either side. Also the instrument can be rotated up or down on the two fixed points (ear and nose). A study of the skull with the instrument in place will show that the second and third branches of the trigeminal nerve are exactly in the axis of the two fixed points (ear and nose) of the instrument, and that the guides point directly to the nerves at all times, regardless of the upward or downward rotation of the instrument. If any bony obstruction is encountered in the passage of the needle while the

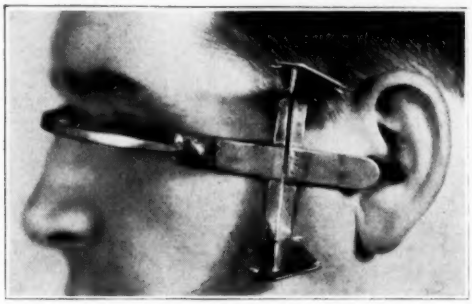


Fig. 2.—Instrument in position for an injection into the trigeminal nerve.

instrument is flat against the zygomatic arch, upward or downward rotation of the instrument will allow the needle to avoid the obstruction.

The guides were placed on the bar at a point of maximum exposure of the nerves. At times it is necessary to have the patient open his jaw slightly in order to allow the needle to pass the upper curved border of the mandible between the coronoid and condyloid processes.

TECHNIC

After putting the instrument in place, a small amount of procaine hydrochloride is injected into the skin at the point where the needle is to be introduced. After waiting a few minutes the needle is introduced, using the grooved guide to indicate the proper direction. The same precautions which experience has shown necessary in alcoholic injection into these nerves must be observed. The needle must not be inserted to a greater depth than 5.5 cm. for the second branch and 5 cm. for the third branch.

The guide does not in any manner displace the skilful, careful neurosurgeon behind the needle. But it is a great aid in indicating the correct angle and direction in which to insert the needle. There are individual anatomic variations, more than 10 per cent, in which the guide does not point directly to the nerve; in such cases the point of the needle will be near, but not in the nerve. In these few cases the guide can be slipped off and the nerve searched for by the old method.

AN EPENDYMAL CYST IN THE QUADRIGEMINAL REGION

Report of a Case

W. B. Hamby, M.D., and W. James Gardner, M.D., Cleveland

Cysts lined by ependymal epithelium and yet isolated from the normal ependymal cavities of the brain are relatively rare. The case reported here is interesting in that the cyst caused central deafness which disappeared after the cyst was opened into the ventricular system.

REPORT OF CASE

History.—A girl, aged 16, came to the Cleveland Clinic on April 5, 1932, because of blindness and deafness. Eight months previously she had fallen from a tree and had been stunned for a few minutes. Failure of vision began soon after this. An ophthalmologist refused to fit her with glasses and made a diagnosis of tumor of the brain, which was not credited by the parents. Four months later she began to have recurring bouts of emesis. She staggered when walking, and had moderate frontal headaches which never became severe. Hearing had failed markedly.

Before the accident the patient had had no illnesses or operations. She had menstruated twice one year prior to the accident, but there had been no subsequent periods. Libido was unimpaired, as the patient stated that during the previous year she had practiced masturbation frequently.

Examination.—The patient was well developed and well nourished, and displayed no visible evidence of endocrine dysfunction. Pressure on the suboccipital regions produced pain on both sides. The eyes were slightly prominent and exophoric. Vision was reduced to perception of light. The disks showed papilledema of 2 diopters, with secondary optic atrophy. The pupillary reactions were sluggish, and the pupils were moderately dilated. Ocular rotations were full in all directions. There was a coarse horizontal nystagmus on lateral rotation of the eyes. The corneal reflexes were active. There was lower facial paresis on the left, the retracted lips and smile being weak, while the upper part of the face reacted normally. Tests for hearing revealed bilateral nerve deafness, more marked on the left. Bone conduction was shortened on both sides; the Weber test was not localized. In the right ear she could not hear C 64, and C 128 was heard very faintly. C 1 was heard rather poorly, while C 2, C 3 and C 4 were heard well. The conversational voice was heard at a distance of 10 feet (3 meters) and the whispered voice at 6 feet (1.8 meters). In the left ear only C 1 and C 2 were heard and these very poorly; conversational voice was heard at 3 feet (0.9 meter) and whispered voice at 1 foot (0.3 meter). An audiogram was attempted, but the patient did not cooperate well enough to complete the study. Caloric vestibular tests yielded hypersensitive reactions. Examination disclosed no dysfunction of the ninth, tenth, eleventh or twelfth cranial nerves.

The reflexes in the upper part of the abdomen were absent; those in the lower part were present and equal. Plantar stimulation caused the toes to fan, but there

From the Department of Neurological Surgery, Cleveland Clinic.

was not a frank Babinski sign. All other superficial and deep reflexes were normal. The patient had a staggering gait, and the Romberg test was mildly positive. Finger-to-nose tests showed incoordination of both hands, more marked on the left than on the right. There was no paresis of the extremities or impairment of deep or superficial sensation.

The spinal fluid pressure was 250 mm. of water. Examination of the fluid revealed no cells and no globulin (Pandy), and the total protein content was 10 mg. per hundred cubic centimeters. The Wassermann reaction and colloidal gold curve were negative, as were the Wassermann and Kahn reactions of the blood. The basal metabolic rate was minus 20 per cent. A roentgenogram of the skull revealed separation of the coronal and lambdoid sutures and a large eroded sella turcica, the floor of which was depressed well into the sphenoid sinus.

Diagnosis.—The clinical diagnosis was obstructive hydrocephalus. The dissociation of auditory and vestibular functions and the fact that the auditory disturbance

Fig. 1.—Ventriculogram before operation, showing dilatation of the lateral ventricles and the anterior part of third ventricle. The large convex filling defect obliterates the posterior part of the third ventricle.

was bilateral indicated a midline lesion. The absence of dysfunction of the fifth nerve in the presence of such marked signs of obstructive hydrocephalus made a lesion of the posterior fossa seem unlikely. Because of the onset of symptoms with amenorrhea and the enlargement of the sella turcica, a juxtasellar lesion was considered probable.

On April 11, a ventriculogram was made under avertin anesthesia, cannulas being introduced into both posterior horns. The ventricles were encountered at less than the usual depth. Ventricular estimation with sodium indigotindisulphonate, U. S. P. (indigo carmine), indicated free communication between the two lateral ventricles. Evacuation yielded 240 cc. of fluid.

The films (fig. 1) revealed a symmetrical, marked dilatation of the lateral ventricles. The anterior portion of the third ventricle was also greatly dilated.

while the posterior portion was obscured by a convex filling defect. The fourth ventricle and aqueduct were not visualized. The diagnosis from the ventriculogram was: tumor in the pineal region with hydrocephalus. It was decided to use a suboccipital approach in performing the operation.

Operation.—With the patient in the craniotomy chair, a suboccipital craniectomy was performed. The cerebellar tonsils were markedly herniated, extending to the second cervical lamina. Both cerebellopontile angles were explored, with negative findings. On inspection, the posterior portion of the fourth ventricle appeared normal. The anterior portion of the ventricle was entirely obliterated, and the lower orifice of the aqueduct of Sylvius was hidden by a downward bulging of the anterior medullary velum. A needle was introduced through the bulging anterior medullary velum, and at once a large amount of fluid was encountered. It was clear and colorless, not being discolored by the dye that was introduced into the

Fig. 2.—Postoperative ventriculogram. The cyst is filled with air.

lateral ventricles at the time of the ventricular estimation. An incision was made into the anterior medullary velum with the electrosurgical needle. The velum was attenuated, and beneath it was the membranous wall of a cyst resembling the arachnoid. A portion of the membrane was excised for microscopic study. The cyst was then examined. The walls, as far as could be determined, were of normal white matter. There was no evidence of neoplasm. A few blood vessels were seen coursing in the walls of the globular cavity of the cyst and no choroid plexus was present. On the superior aspect, running in an anteroposterior direction, were paired veins resembling the veins of Galen. No opening could be demonstrated in the cavity. After the cavity had been inspected, an attempt was made to demonstrate the aqueduct, but this was not accomplished because of the difficulty in retracting the sagging cyst wall. It was the surgeon's impression that the aqueduct lay beneath the cyst. The wound was closed in tiers with silk sutures and without drainage. Following the operation, more ventriculograms were made in order to demonstrate the cyst, which now contained air (fig. 2).

Anatomic Diagnosis.—The postoperative diagnosis was arachnoid cyst or obstructed accessory ventricle in the quadrigeminal region.

Histologic examination of the removed portion of the wall of the cyst showed a strand of tissue consisting of loosely arranged, vascularized, collagenous stroma on one surface and a single layer of flattened cuboidal epithelial cells on the opposite surface. Between the surfaces was a layer of cerebral glial tissue, not neoplastic. The histologic diagnosis was: a cyst wall lined by ependyma (fig. 3).

Course.—The postoperative course was at first stormy; the temperature reached 106 F. on the night of the operation. The patient improved steadily thereafter, although several ventricular punctures were performed to relieve increased intracranial pressure.

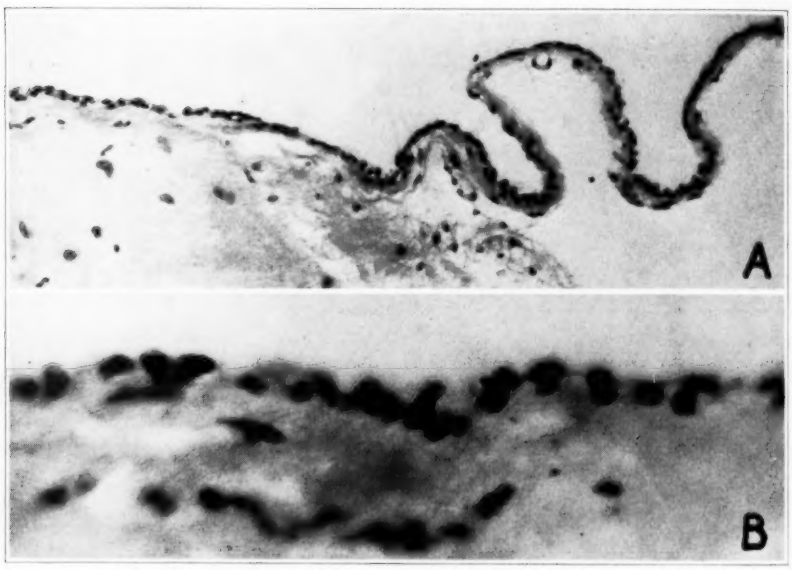


Fig. 3.—Photomicrographs of the wall of the cyst, showing, *A*, a layer of flattened epithelial cells on a glial base (× 100), and *B*, the same in higher power magnification (× 500).

The patient was discharged on May 1, twenty days after the operation, when hearing was definitely improved, especially on the left side. Although the edema of the optic disks had receded, vision was still limited practically to perception of light. She was incontinent and incoordinate, unable to walk or to hold her head erect. When she was seen again, forty-five days later, the incoordination had diminished markedly and she was able to walk with confidence. She was entirely continent. Hearing had returned practically to normal: an audiogram showed marked improvement; whispered voice was heard at 10 feet and conversational voice at 15 feet (4.5 meters) in each ear. The menses had not reappeared. Ten months after operation, the patient was in a school for the blind. The physicians in charge reported that she was in excellent health. Vision was restricted in each eye to perception of hand movements. The right pupil was slightly larger than

the left, and both reacted promptly but incompletely to light, directly and consensually. There was no papilledema, but a pronounced secondary optic atrophy was present. Conversational voice was heard without difficulty, and an audiogram revealed a normal hearing range (fig. 4).

COMMENT

The nerve deafness in this case was due to the strategic location of the lesion. Horrax and Bailey,[1] in reporting twelve verified cases of pineal tumor, reviewed the neurologic signs of involvement of the quadrigeminal plate. According to them, paralysis of the third nerve is a prominent finding, and is usually manifested by paralysis of the upward gaze or by pupillary disturbances. In our patient,

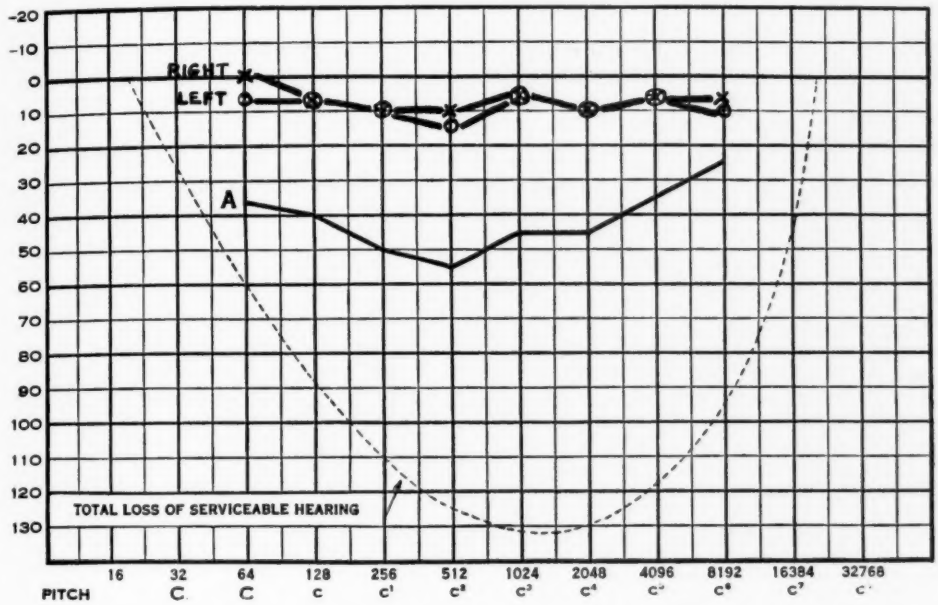


Fig. 4.—Audiogram, showing the normal range of hearing ten months after the operation. Zero indicates normal hearing, and the sections below indicate the loss of hearing as measured in units of sensation. The percentage loss of hearing for speech is approximately equal to the average reading at 512, 1,024 and 2,048 multiplied by 0.8.

exophoria was the only evidence of faulty innervation of the eye-muscle. The dilated, sluggish pupils were attributed before operation to the relative amaurosis, an impression which the postoperative course confirmed.

Bilateral central deafness of varying degrees was found in five of their twelve patients and was the most striking feature in our case. This interesting bilateral dissociation of auditory and vestibular function is due to pressure of the lesion

1. Horrax, G., and Bailey, P.: Tumors of the Pineal Body, Arch. Neurol. & Psychiat. **13**:423 (April) 1925.

on the quadrigeminal plate, where the inferior quadrigeminal bodies receive fibers from the lateral lemniscus, the connecting link between the cochlea and the cortex.[2] Prompt return of auditory function was possible in our patient, as the nature of the lesion permitted complete relief of the pressure on the quadrigeminal plate without the destruction of tissue.

Horrax and Bailey also mentioned that in such cases there are evidences of indirect involvement of the cerebellar tracts. This was probably responsible for the staggering gait and the mild Romberg sign displayed by our patient.

The amenorrhea was probably secondary to the obstructive hydrocephalus. The symptom is frequently encountered in young women with this lesion. Its mechanism is not definitely established, but seems most likely due to disturbance of the pituitary gland incident to direct pressure of the dilated third ventricle on the gland, or possibly to disturbances of the hypothalamic-hypophyseal neural connections.[3]

In considering the origin of the cyst lined with ependyma, three possible sites suggest themselves: the pineal body, the cavum Vergae or so-called sixth ventricle, or an embryonal rest of ependymal cells in the region of the quadrigeminal plate.

Cysts of the pineal body are not uncommon.[4] They are usually small, and pineal tissue is readily recognizable in their walls. The cyst in this instance, however, was huge, and it is hardly conceivable that the attenuation of pineal tissue could result in such a perfect layer of simple cuboidal epithelium, typical of ependyma.

A cyst of the cavum Vergae was considered, such as Dandy [5] has reported. He considered all openings into these cysts as purely artificial. The so-called accessory ventricles are extraventricular and hence should have no ependymal lining. Dixon and Ebaugh [6] reported a case in which a cyst of the cavum septi pellucidi was in communication with the third ventricle via a small opening in the roof, and encephalographic visualization was made of the cyst. They did not mention the character of the lining cells, and there is little in the literature concerning the histology of the lining of the so-called accessory ventricles. Dandy [5] quoted Dejerine, Poirier and Charpy as stating that ependyma and choroid plexus are lacking in the cavities. Our studies on the simple cavum septi pellucidi showed the lining of the cavity to be merely attenuated neuroglia, with no evidence of ependyma (fig. 5). The development of an ependymal cyst from these cavities seems unlikely.

Another possible explanation of the origin of the cyst is suggested by the report of a similar one by Vítek, Sachs and Jedlička.[7] Their patient, a man, aged

---

2. Bailey, P.: Intracranial Neoplasms, Springfield, Ill., Charles C. Thomas, Publisher, 1933, p. 332. Tilney, F., and Riley, H. A.: Form and Functions of the Central Nervous System, ed. 2, New York, Paul B. Hoeber, Inc., 1923, p. 493.

3. Fulton, J., and Bailey, P.: Tumors in the Region of the Third Ventricle, in Relation to Pathological Sleep, J. Nerv. & Ment. Dis. **69**:1, 1929.

4. Globus, J. H.: Pinealomas, Arch. Neurol. & Psychiat. **25**:937 (May) 1931. Handley, R.: Pineal Cysts, with Report of Two Cases, J. Ment. Sc. **76**:250, 1930.

5. Dandy, W. E.: Congenital Cerebral Cysts of the Cavum Septi Pellucidi and Cavum Vergae, Arch. Neurol. & Psychiat. **25**:44 (Jan.) 1931.

6. Dixon, H. H., and Ebaugh, F. G.: Encephalography, Arch. Neurol. & Psychiat. **28**:1326 (Dec.) 1932.

7. Vítek, J.; Sachs, A., and Jedlička, V.: Subacute Compression of Aqueduct of Sylvius by Ependymal Cyst, Casop. lék. česk. **68**:1673 and 1730, 1929.

22, presented a bizarre neurologic picture. A left frontal craniotomy was performed; the lesion was not found, and the patient died. At necropsy an enormous obstructive hydrocephalus of the lateral and third ventricles were exposed. In the right thalamus was a cyst, the size of a prune, obstructing the aqueduct by pressure. The walls of the cyst were tough and well supplied with blood vessels; it was lined with a smooth membrane. It contained no choroid plexus and had no connection with the ventricles. Histologic examination showed the lining membrane to be ependymal epithelium, cuboidal or flattened, with a few ciliated cells. Between the wall of the cyst and the lateral ventricle was a small cluster of neuroglial and cuboidal cells of the ependymal type.

The authors interpreted the changes as showing that an evagination of the right lateral ventricle had been isolated in the thalamus and the communication

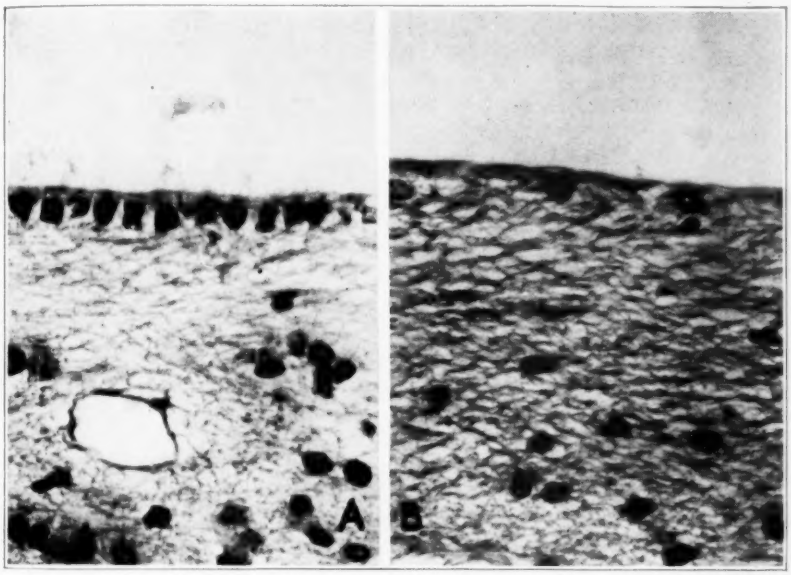


Fig. 5.—Cavum septi pellucidi. *A* shows the ependyma of the adjacent lateral ventricle. Fincher's silver carbonate (Fincher: Am. J. Cancer **16**:918, 1932); × 500. *B* shows the lining of the cavum septi pellucidi. No epithelium covers the flattened neuroglia cells on the surface. Fincher's silver carbonate; × 500.

obliterated until only a small island of tissue remained. Increase in the size of the cyst led to the dislocation and compression of the median nucleus of the thalamus, which was forced over slowly, closing the aqueduct, and led to a gradually increasing hydrocephalus, which was of long standing at the time of examination.

While the location of the cyst was not entirely similar to that in our case, its effects were much the same, and the methods of formation of the two were possibly similar. It is conceivable that in our patient some such process occurred near the quadrigeminal plate, resulting in the formation of a cyst. The later increase of fluid within the cyst must have come from either transudation through or secretion by the ependyma, since careful inspection of both cysts revealed no other

source. Analysis of the fluid of the cyst revealed 1 cell, a negative globulin (Pandy) reaction and less than 10 mg. of total protein. That the fluid might have come from the ventricles by direct communication seems unlikely, not only because careful inspection of one wall of the cyst failed to reveal an opening, but also because the dye injected into the lateral ventricles did not enter the cyst. Moreover, the perfectly globular shape of the cavity suggests that its internal pressure was greater than the general intracranial pressure.

In our case, it is an open question whether the fall, with its incident trauma, initiated the abnormal accumulation of fluid or whether the fall was caused by asynergia resulting from pressure of the cyst on the cerebellar tracts.

SUMMARY

A case is presented of a large ependymal cyst compressing the quadrigeminal plate.

Bilateral central deafness was relieved by evacuation of the cyst.

Amaurosis was permanent, because of secondary optic atrophy.

The cyst did not refill after the fistula into the fourth ventricle was provided.

A possible explanation offered for the formation of such cysts is that by the occlusion of the neck of a diverticulum from a ventricle an island of ependymal cells was isolated in the brain tissue.

A CASE OF PSYCHOSIS ASSOCIATED WITH MIDLINE CEREBELLAR TUMOR

LEO STONE, M.D., AND WILLIAM C. MENNINGER, M.D., TOPEKA, KAN.

The occurrence of mental symptoms in tumors of the frontal lobe is sufficiently frequent to have established a widely recognized clinical syndrome. Whether the mental symptoms of lesions of the frontal lobe are evidences of focal destruction alone is not certain, but they are so regarded by the majority of observers. With increasing interest in the psychiatry of cerebral tumors it has become apparent that mental disturbances may arise in the course of tumors in other portions of the brain, and that such disturbances cannot always be attributed to a high degree of intracranial pressure, a factor which may, of course, give rise to some degree of mental hebetude in any patient. Perhaps excepting the corpus callosum, however, the frontal lobes remain the portions of the brain which are most liable to respond to neoplasms with early and predominant alterations in personality or in personality or intellect.[1] When such changes present themselves in a case of tumor of the brain, the clinician is liable, on a statistical basis, to give the frontal lobes too firm a place in his differential diagnosis. Such an attitude is not universally held, however, and it has been affirmed that mental symptoms in tumors of the brain arise as a reaction in personality due to widespread disturbance in the brain, that mental symptoms are not, in fact, the most important early manifestations even in tumors of the frontal lobe.[2]

Regardless of the mechanism involved, it is well established by experience that mental disturbances are rare in tumors of the posterior cranial fossa.[3a] When they do occur they are usually the obvious sequelae of long-standing intracranial hypertension, and they are preceded by a train of symptoms which, if not of clear topographic significance, are at least indicative of severe intracranial pressure.[4] Symptoms and signs of severe intracranial pressure are always suggestive of a lesion of the posterior fossa and, from the negative point of view, are not nearly so common early in the course of expanding lesions of the anterior portions of the brain. The objective data from examination, furthermore, sometimes indicate conclusively the location of the tumor. The anamnestic or examinational data

---

From the Menninger Clinic.

1. Discussion on: Mental Symptoms Associated with Brain Tumours, Meeting of the Sections of Neurology and Psychiatry, Royal Society of Medicine, Lancet **1**:408 (Feb. 21) 1931.

2. Kubitschek, P. E.: The Symptomatology of Tumors of the Frontal Lobe; Based on a Series of Twenty-Two Cases, Arch. Neurol. & Psychiat. **20**:559 (Sept.) 1928.

3. (*a*) Wechsler, I. S.: A Textbook of Clinical Neurology, ed. 2, Philadelphia, W. B. Saunders Company, 1932, pp. 482, 489 and 513. (*b*) Moersch, F. P.: Psychic Manifestations in Cases of Brain Tumors, Am. J. Psychiat. **4**:705 (April) 1925. (*c*) Southerland, R. W.: Three Cases of Tumors in the Posterior Cranial Fossa with Mental Symptoms, Bull. Neurol. Inst. New York **2**:144 (March) 1932.

4. Henry, G. W.: Mental Phenomena Observed in Cases of Brain Tumor, Am. J. Psychiat. **12**:415 (Nov.) 1932. Discussion.[1] Southerland.[3c]

accompanying a psychotic syndrome may thus deprive the mental symptoms of much of their false localizing significance.

Occasionally signs of localizing value in cerebellar tumors may diminish or disappear as the disease progresses.[5] Even less frequently a cerebellar tumor may lack from the onset the characteristic evidences of its location, or may present them to such a slight degree that they are disregarded by both patient and family in giving the history and are not available to the examiner when the patient is first seen. When such a case presents a fully developed syndrome of organic mental deterioration, including *Witzelsucht*, the difficulty of correct localization is obvious. The following case presented a frontal lobe syndrome due to a large midline cerebellar tumor, with an almost total absence of data from anamnesis or examination indicating its actual location. Similar cases have been described,[6] but it is thought that the clinical syndrome is sufficiently instructive to merit individual report.

REPORT OF A CASE

History.—A woman, aged 57, who had been born in Germany and had come to this country at the age of 16, had two brothers living and well and another who had died of heart disease two years before the patient's illness. At the age of 26, she had married, but divorced the husband at the age of 40 for infidelity. During most of the time since she had worked as a clerk in a dry goods store in a small city. The marriage was a painful memory and she refused to speak of it, although the brothers suspected that she often brooded on the subject. She had, indeed, told a neighbor that since the trouble with her husband she had been subject to pain in the back of the head and flushing of the face whenever she became excited. No important illnesses were recalled; the patient had a "jolly" temperament and was well liked. She had no male acquaintances outside her family, but went out a great deal with women friends and frequently visited her brothers. The patient had been deeply moved by the brother's death, and had occasionally expressed great concern over the alcoholic tendencies of some nephews, but she had never shown any appreciable change in behavior until the final illness began.

In the winter of 1931-1932 the patient began to be "careful of her eating," apparently because of constipation. During the summer, 1932, a bolt of goods fell on the back of her neck while she was at work, throwing her to the floor but leaving no important ill effects. Around Thanksgiving, 1932, the patient complained frequently of her "stomach," again principally because of constipation. It was certain that she did not vomit. About Jan. 1, 1933, the patient began to complain vaguely of fatigue and mental inadequacy. Shortly thereafter she had a sudden attack of dizziness and "nervousness" in the store, followed by a brief fainting spell. The patient considered herself overworked, and told her brothers that her whole trouble lay in the fact that she "killed herself working and got no thanks for it." From the beginning of the illness the patient's memory was impaired and she showed frequent confused rambling in her speech. She would wander from a subject and then ask, "What am I talking about?" At the onset

5. Wechsler.[3a] Hausman, L., and Stevenson, L.: Astrocytoma of the Cerebellum: Survival Period of Forty-Five Years Without Operation, Arch. Neurol. & Psychiat. **30**:1100 (Nov.) 1933.

6. (*a*) Adelstein, L. J., and Carter, M. G.: Psychosis: Its Importance as a Presenting Symptom of Brain Tumor, Am. J. Psychiat. **12**:317 (Sept.) 1932. (*b*) Discussion.[1] (*c*) Southerland.[3c]

of the illness the patient complained frequently of headache and dizziness, but these symptoms disappeared entirely after five or six weeks. There were no motor disturbances of any kind in the early weeks of the disease. There was, however, progressive general weakness and emaciation and, two weeks before coming to Topeka, she began to stagger because she was "so weak." At this time she was ordered to bed for a rest by her physician. (It is worthy of special note that the headache and staggering were denied by the patient's brothers even after the autopsy. The history of these symptoms was elicited in an interview several months after the patient's death.)

From the beginning of the illness the patient joked and laughed excessively, but the brothers considered these phenomena in keeping with her original temperament. Despite this tendency the patient was greatly concerned about her mental inadequacy for work. A rest which had been recommended gave no improvement. During her absence from work she complained to another woman with whom she had been living that she feared the inventory at the store could not be completed without her. Her manner gave the companion the impression that the remarks were based on delusion. She expressed other more definitely mistaken ideas and was accordingly hospitalized for a week. For three weeks thereafter she remained in a nursing home. She began to express delusions of people dying and referred especially to her brother, despite his frequent visits. Periodically she became disoriented and confused, and gradually worse in general. A local physician made the diagnosis of a nervous breakdown due to overwork. Later he thought it was probably a "softening of the brain." The patient was admitted to St. Francis Hospital, Topeka, under the care of Dr. Thomas O'Connor. After admission she spoke to the nurse about wanting a baby but not being old enough to have one.

Examination and Course.—On March 10, 1933, when examined by us, the patient was lying in bed and looking blankly at the ceiling. She was emaciated. Her only greeting was, "Well, where did you come from?" Her attention was gained with difficulty; her voice was feeble and her responses sluggish. She identified the examiner as W. S., a man who had traded at her store, and insisted that she was in the store at the time. She stated that she was in bed because the "others" thought her sick, then added that she was in the courthouse "because she was being questioned" and that she had been out of work for eight months. Speech was disconnected. Her answers were only occasionally relevant. She was disoriented in all spheres. Pathologic euphoria was frequently evident. At one time she bit her lower lip, grunted, expelled gas from the anus, and then asked the examiner with a smile, "Did'you get that?" She did not cooperate in the examination but was not actively resistive.

On neurologic examination the optic disks were poorly seen because of continual motion of the eyes; the veins of the left disk were apparently full and its margins indistinct; the left pupil was larger than the right and both were in mid-dilatation; in the first test, the pupils were nearly fixed to light but fifteen minutes later they responded promptly. There were: a moderate left facial weakness of central type, an apparently symmetrical general muscular asthenia and a marked symmetrical exaggeration of the tendon reflexes. The patient did not cooperate in the sensory tests or tests for coordination. No nystagmus, ataxia or incoordination was evident in spontaneous movements.

The tentative opinion from this examination was that the patient was suffering from an organic psychosis, associated either with dementia paralytica or a tumor of the brain. A roentgenogram of the skull, serologic study of the blood and examination of the spinal fluid were advised, and the findings were reported as normal.

On March 13 the patient was seen again. She was lying quietly in bed and was incontinent of urine; the right arm was in a hemiplegic position and was painful on any motion. The tendon reflexes were symmetrically hyperactive, with an inconstant bilateral ankle clonus. However, there was a definite Babinski sign on the right. The abdominal reflexes were obtained only as quickly exhaustible flickers. The right nasolabial fold showed very slight smoothing. The left pupil was larger than the right; both were somewhat irregular and reacted sluggishly to light. Both ocular fundi showed beginning papilledema with dilatation and tortuosity of the veins. There were no hemorrhages or exudates. The protrusion of the disk could not be measured because of ocular restlessness, but it was obviously slight. The patient did not cooperate in the finger test for estimation of the visual fields; she did not even respond to threatening gestures. She did not cooperate for tests of sensation or coordination. A marked distractibility and lassitude were evident at this examination. The opinion following this examination was that the patient had a deeply placed tumor of the left frontal lobe.

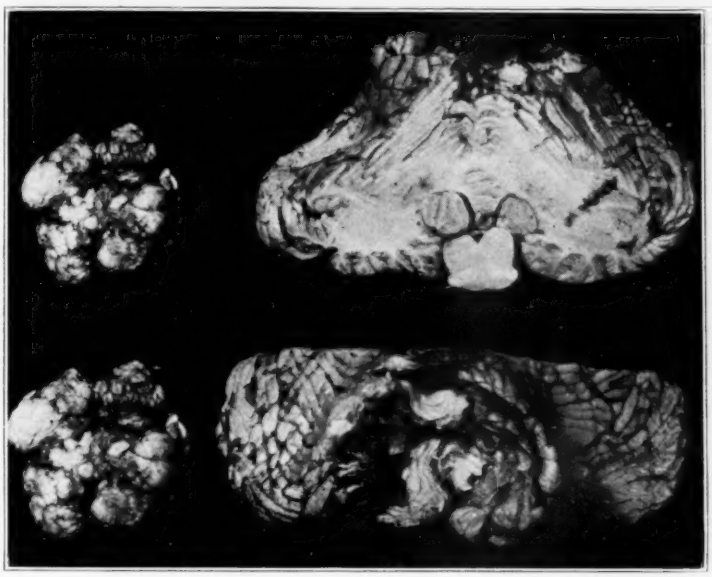
On March 17, examination revealed a distinct right hemiparesis with Babinski's sign. The tendon reflexes, however, remained symmetrically hyperactive, the hyperactivity being much more marked in the lower extremities. The abdominal reflexes were obtained as quickly exhaustible flickers on the right; they were absent on the left. Slight smoothing of the right nasolabial fold was again evident; it was not accentuated by either emotional or volitional movement. The patient said that she perceived odors equally on both sides; however, she did not name them. The ocular fundi were as described previously; the elevation was less than 1 diopter. The left pupil was larger than the right; both reacted normally. There was apparently partial bilateral ptosis. The corneal reflexes were present bilaterally. No form of sensory examination yielded valid findings, not even the pin prick. If anything, the patient felt the pin better on the hemiparetic side, although she frequently transposed sides and at times felt the pricks equally well on both sides. Speech was often grossly confused and the patient frequently misnamed common small objects, such as a watch chain or knife. She executed simple commands referable to the right or hemiparetic arm quite well. The left arm, which was quite strong, would often remain motionless in response to a simple command, such as, "Put your finger on your nose." On occasions there would be an abortive, ineffectual twisting movement of the arm. Grasping reflexes were present bilaterally, as well as a marked tonic perseveration. These were more marked on the right. There was gross incontinence of urine. The patient was emaciated and unable to rise from bed. She responded to no commands involving the legs. There was no nystagmus. Tests for coordination in the right upper extremity were satisfactory; in the left there was an apparent apraxia.

The impression at this time was that the patient was suffering from a tumor of the left frontal lobe, deeply and medially placed, possibly with considerable destruction of the anterior portion of the corpus callosum. Exploratory craniotomy was advised, but the recommendation was not accepted.

On April 19 (the fortieth day in the hospital), few of the patient's responses were rational. She required feeding by nurses, who had to open her mouth forcibly at times. The patient was frequently facetious about the examination. She laughed often; once she nearly cried. The bilateral papilledema was slightly more marked. The right arm was extremely weak, the left considerably stronger. She would occasionally pick up things with the left hand on command; more often she would not. She made no voluntary movements with the right hand. The difficulty in naming objects persisted, with an obvious element of perseveration. She would continue to call simple objects by the same name used for a previous test, whether

correct or incorrect. All tendon reflexes were greatly exaggerated, more so on the right. There was a bilateral Babinski sign. The patient was incontinent of urine and feces. The grasping reflex was present bilaterally, being now more marked on the left.

On May 24, emaciation was severe. The patient made few remarks, and there was considerable clouding of consciousness. She lay on the left side, with the legs flexed and the knees separated by a pillow. Any attempt to move any part of the body except the left arm resulted in pain. The choking of the disks was considerably greater than before. The left pupil was noticeably larger than the right. There was only slight flattening of the right nasolabial fold. The right arm could not be moved at all. The left arm could be moved slightly, but was never used. The grasping reflex remained strong in the left hand, but was feeble in the right.



Cerebellum and medulla in a case of midline cerebellar tumor seen in vertical section and from the superior surface, with the detached tumor shown at the left. Note the excavation made by the tumor.

All tendon reflexes were obtained with difficulty, except the ankle jerks which remained brisk, and there was a bilateral Babinski sign. The flexion of the legs could not be broken. In the interval the patient had had for a time a temperature of from 100 to 104 F., but this had subsided at the time of examination.

Progressive general weakness continued, with irregular fever up to the patient's death on June 21, 1933.

Autopsy.—The brain exhibited marked general edema. On palpation there was evident internal hydrocephalus, more marked in the left cerebral hemisphere. The frontal and occipital poles in both hemispheres were rounded. There was a small amount of clotted blood in the region of the cisterna magna. The floor of the third ventricle bulged markedly, imparting a cystic appearance to the region of the tuber cinereum. Attached to the meninges of the posterior fossa, but lying

predominantly in the posterior superior portion of the cerebellum, was a firm tumor with an irregular nodular surface, about the size of a small hen's egg. The tumor had destroyed the greater part of the vermis and had encroached equally on both cerebellar hemispheres to a depth of about 1 cm. The tumor was encapsulated and easily separable from the surrounding tissue.

The brain was cut vertically after hardening in a 10 per cent solution of formaldehyde. Sections revealed dilatation of the entire ventricular system, extending back to the posterior portion of the fourth ventricle where the tumor exerted its maximum pressure. The dilatation was somewhat more marked in the anterior horn of the left lateral ventricle. The tumor in section was firm and grayish with numerous dilated blood vessels and petechian hemorrhages. Microscopically (Dr. Charles Davison, New York), the appearance was that of a highly cellular meningioma. Inspection of the remainder of the brain revealed no gross evidence of intrinsic disease. Sections from the prefrontal cortex and subcortex on both sides showed no alterations on microscopic examination beyond slight edema.

COMMENT

It is evident from the postmortem examination that the primary anatomic cause of the patient's symptoms was the midline cerebellar neoplasm, and that the immediate cause was the internal hydrocephalus. The latter agent was, for unknown reasons, most deleteriously effective on the tissues subserving intellectual functions, presumably the frontal lobes. No active contributing disease was evident in this region. It is possible that a primary vulnerability of the tissue was the factor which caused the frontal lobes to present early and striking alterations in function in the presence of increased intraventricular tension. Nor can one overlook the fact that a purely psychologic inclination to mental disorder in this patient may have been speedily activated by a definite pathophysiologic change, that is, by increased intracranial pressure. Such a mechanism may also be responsible for the striking psychotic syndromes observed at times in uremia, influenza, lobar pneumonia and other infectious and metabolic disorders.

Of great interest in this case was the presence of aphasia. This was predominantly of the nominal (sensory) type, but aphasia of this type has occurred in verified tumors of the frontal lobes.[7] This symptom, with the apparent apraxia and the grasping reflexes, was undoubtedly of the same origin as the intellectual disturbances. It is possible that the "apraxia" represented an extreme degree of cerebellar asynergia.

When this patient was first seen there were no positive evidences of cerebellar disease, unless primary emaciation without vomiting is considered an important cerebellar symptom. Headache and dizziness did occur very early in the course of the disease, only to disappear entirely later. Vomiting never occurred. Choked disk was of a very low grade until shortly before death. The disturbance of gait occurred only when the disease (with general emaciation and asthenia) was well advanced. The occurrence of ataxia is not rare in tumors of the frontal lobe, and is often accompanied by other evidence of disturbance of the frontopontocerebellar pathways. The failure to elicit a history of headache and staggering by direct questioning at the time of examination may denote an error on the part of the informant, or possibly of the recorder, but it also implies the relative inconspicuousness of these symptoms. In the hydrocephalus of tumors of the posterior fossa symptoms of increased intracranial pressure are usually early and striking.

7. Sachs, E.: Symptomatology of a Group of Frontal Lobe Lesions, Brain **50**:474 (Oct.) 1927.

It is true that this patient was seen in a stage of the illness when cerebellar signs and symptoms formerly present may have been no longer demonstrable, and when the patient herself was no longer capable of giving reliable information. If this were not true, one would have to postulate a striking resistiveness of the cerebellar tissues in contrast to the marked vulnerability to pressure of the frontal lobes.

That the tumor was large considering the duration of the symptoms may lend added significance to the "nervous" occipital headaches of the past and to the blow in the same region which had been received while at work. The latter may have caused an increased rate of growth in a silent tumor of long standing.

One may ask how the inaccurate diagnosis made in this case might have been averted. The objective clinical syndrome was that of a tumor of the left frontal lobe, and the history supported this localization. An exploratory craniotomy in this region would have revealed the evidence of internal hydrocephalus, which would have directed attention to the posterior fossa. A ventriculogram preceding operation would certainly have demonstrated the ventricular dilatation characteristic of neoplasms of the posterior fossa. This procedure has been indispensable to correct diagnoses in similar cases.[8]

SUMMARY

1. A case of midline cerebellar tumor with marked internal hydrocephalus is described, with the postmortem observations. The case presented a syndrome highly suggestive of a neoplasm of the left frontal lobe with a notable inconspicuousness of cerebellar signs or evidences of the high intracranial pressure characteristic of subtentorial tumors in general.

2. The possible dynamics of the hydrocephalic mental syndrome are mentioned with reference to organic vulnerability of the frontal lobes, to psychopathologic predisposition and to unusual resistiveness of the cerebellar pathways.

3. The clinical problem involved in such a case is considered, especially the need for ventriculography.

CONCLUSIONS

1. A psychosis may be the presenting clinical problem in cerebellar tumor, and all conclusive manifestations of cerebellar tumor may be lacking at the time when the patient is seen.

2. Topographic diagnosis is always difficult in cases of advanced tumor of the brain, and more difficult than usual when a psychosis excludes the possibility of a reliable subjective account of the disease. Erroneous topographic diagnosis is an especially great hazard in such cases, even when an apparently well defined clinical picture is present. Ventriculography should be employed to avert such an error.

---

8. Adelstein and Carter.[6a] Southerland.[3c]

Abstracts from Current Literature

THE VESTIBULAR FUNCTIONS OF THE FRONTAL LOBE WITH THE STRIATED BODY: CEREBRAL AND SUPRATENTORIAL ATAXIA. L. J. MUSKENS, Rev. d'oto-neuro-opht. **12**:1 (Jan.) 1934.

The reasons that the functions of the frontal lobe are so poorly understood are neglect of the principle of Griesinger (anatomy first, physiology next and then the clinical picture), brutal methods of intervention on the frontal lobe and the ignoring of vestibular and supravestibular disturbances, especially those occurring in an anteroposterior direction. Frontal ataxia is not a true ataxia, a tabetic dysmetria or a true incoordination but comprises the symptoms accompanying attitudes or forced movements and the concomitant oculomotor manifestations in the vertical plane.

Clinical experience teaches that every organic disease in the anterior part of the brain disturbs the function of the anterior part of the striatum and vice versa; anatomic investigation shows that the blood supply of the anterior part of the brain is such that destruction of the basal part of the frontal lobe must necessarily block certain arterial territories in the pallidum.

The following assumptions are justified: The striate body is a major center for the production of automatic movements; the globus pallidus is a supravestibular organ; the pallidum (paleostriatum) is the principal center of association and is developed concurrently with the frontal cortex; the putamen and the caudate nucleus (neostriatum) are its physiologic and histologic counterparts; there are pathways of association between the cortex and the thalamus, between the paleostriatum and the neostriatum, between the globus pallidus and the body of Luys and between the pallidum and the vertebral trunk. Consequently, the neostriatum is an organ of sensory correlation, grouping various centripetal influxes, and the paleostriatum is an organ of sensory execution.

In all cases, branches of the anterior cerebral artery terminate in the globus pallidus, and they are certainly cut or blocked during an intervention involving solely the frontal cortex. When, therefore, typical striatal symptoms appear following such intervention, they should be attributed to these inevitable striatal foci. This fact speaks against the assumption of direct relations between the cortex and the pallidum. Hoche's researches showed that pyramidal fibers terminate in the motor nuclei of the fifth, seventh, eleventh and twelfth nerves, but none have been found in those of the third, fourth and sixth nerves; Muskens remarks that the rôle of the striatum in ocular movements has been underestimated. There exists no incontestable result from experimentation, anatomic or physiologic, that obliges one to accept the existence of supravestibular functions in the frontal cortex.

From a clinical point of view, the reports of frontal ataxia by numerous authors are criticized. Bruns and Oppenheim first insisted on the regular occurrence of ataxic phenomena in patients with frontal tumors: instability of the body, staggering and reeling and a tendency to fall backward. The belief of Subirana that the "small step" gait is a vestibulospinal syndrome is not concurred in. The hypothesis that ataxia in cases of supratentorial tumors is caused by a "pressure cone" is not accepted, because ataxia has no localizing importance unless it appears early and because in numerous cases the pressure cone was lacking. The fact that in cases of supratentorial tumors median tumors cause ataxia oftener than lateral tumors is comprehensible if one attributes the principal rôle to the frontopontocerebellar tract or to the neostriato-olivary bundle (Muskens); the frontopontocerebellar tract probably does not exist.

When investigating the functions of the anterior part of the brain, physiologists have too little taken into account the various nuclear and fascicular complexes

and the existence of supravestibular centers in the striatum. Muskens showed in 1914 that *mouvements de ménage* persist for months and are produced only after wounds of the anterior part of the brain involving the globus pallidus. Schäfer, Sherrington and others showed that the prefrontal electrically excitable zone was without connection with the motor zone and that stronger faradic currents were necessary to stimulate the frontal cortex than for the central convolutions. Conjugate deviation of the head and eyes from stimulation of the frontal lobe can be attributed only to stimulation, by diffusion of the current, of the subjacent striated formations. In electrical stimulation of the central ganglia, *mouvements de ménage* were produced to the diseased side and were accompanied by a tendency of the patient to fall to the healthy side. One of the most constant symptoms after a deep wound of the anterior part of the brain is a tendency of the patient to fall toward the healthy side (modified rolling movement); other forced movements (*mouvements de ménage* toward the wounded side, retropulsion, propulsion and oblique gait) were also observed. Edwards and Bagg observed that the necrosis from radium was manifested only on the putamen and the caudate nucleus—never on the pallidum—and provoked trembling but not rotation or *mouvements de ménage*. These observations confirm Muskens' ideas as to the rôle of the pallidum. One of the most important causes of the confusion that existed between physiologists and clinicians was the lack of consideration of the tendency of the patient to rotate to the healthy side and of forced movements in the vertical plane after a lesion of the anterior part of the brain. In 1914, Muskens showed that following systematic hemisection of the posterior longitudinal bundle the point where direction of forced movements of rotation and *ménage* is inverted was at the posterior commissure, where the ascending fibers decussate (especially the vestibular fibers); that the posterior commissural nucleus and the commissuromedullary tract are the principal elements in locomotion and ocular movements in the horizontal plane; that *mouvements de ménage* toward the right could be provoked not only by a lesion of the right posterior commissural nucleus but by one of the right globus pallidus and the pathways uniting these centers. Lasting *mouvements de ménage* were established only if the lateral part of the globus pallidus was wounded. Other lesions of the anterior part of the brain were followed only by transient *mouvements de ménage*. Analogous observations on forced movements in the frontal plane were made. The interstitial nucleus and the spinal tract direct movements of rotation toward the healthy side with a tendency to falling and the ocular deviation of Hertwig and Magendie; the nucleus is united by ascending and descending fibers with the anterior part of the globus pallidus. An extended lesion of this portion, associated or not with a lesion of the lenticular nucleus or of the putamen, is followed by a durable tendency to rotation and falling to the healthy side. The results of Morgan's researches on sections of the striatum agree with those of Muskens.

DENNIS, Colorado Springs.

ANOMALIES OF THE OCULAR MUSCLES. ALEXANDER DUANE, Arch. Ophth. **11**:394 (March) 1934.

From time to time brief reviews have been presented of certain sections of the unpublished work of Dr. Alexander Duane on the ocular muscles, work that was incomplete at his untimely death. Through the courtesy of Mrs. Duane these sections have appeared in the *Archives of Ophthalmology*. They represent the views of an authority who devoted his life to scientific research in a field to which he ably contributed. The present article considers the symptoms and diagnoses of anomalies of the ocular muscles as they apply to paralysis and spasm. It is unfortunate that this section does not lend itself well to abstracting. Certain subsections, however, will be taken from the work and presented. The reviewer believes that the article, for obvious reasons, should be read in the original.

Some of the subsections deal with the essential identity of symptoms in underaction and overaction, however caused; paralysis and spasm and, in connection with them, the equivalence of the effect produced by paralysis of one

muscle and by spasm of its associate and the objective evidences of paralysis or spasm; lagging or overshooting, and noncomitant deviation. The subjective symptoms of paralysis and spasm are considered as well. In this group there are certain basic factors of importance. Paralysis of a muscle in one eye is invariably the cause of a spasm of its associate in the fellow eye. Such a secondary spasm of the associate muscle is usually seen in conjunction with paralysis whenever the paretic eye fixes. Certain definite symptoms are common and characteristic, for instance, a sense of discomfort in moving the eye, false projection, the different movement of objects, varying types and degrees of diplopia, vertigo and confused vision.

The attitude of the head in oculomotor paralysis, i. e., ocular torticollis, deserves special attention, not only because of the diagnostic significance attributed to it, but because not infequently it is so disfiguring and produces so much discomfort that it calls for relief on its own account. This is evidence of the attempt to relieve part of the subjective symptoms which the patient has, and it is discussed in detail with the presentation of certain illustrative cases.

The variation of symptoms in individual cases is marked: 1. The mistakes in projection, particularly as they make their appearance in the past-pointing test, gradually cease; the patient learns by experience that the impulses of innervation from his paralyzed eye correspond to a much slighter action than those for the sound eye, and by taking account of this fact he once more forms a correct judgment of the situation of objects. 2. The diplopia may disappear through suppression, although such suppression is rarely complete and in many cases does not occur. However, though not actually eliminated, the diplopia after a time becomes much less obtrusive and annoying. 3. It often happens that, owing to contracture of the antagonists of the paralyzed muscle and other changes, the deviation and diplopia increase in amount and become apparent not only in the field of action of the paralyzed muscle but also in the field of action of its antagonist, and they may even extend so far over the whole field of fixation that a paralytic strabismus may come to resemble an ordinary concomitant squint. In proportion as it does so, the symptoms grow less disturbing; for, as already stated, it is always the case that, other things being equal, a concomitant deviation will give less trouble than will one that is nonconcomitant.

Variations which are so constant are likely to be a disturbing factor in the study of any one case. The diagnosis of ocular paralysis and of ocular spasms is considered in a systematic fashion. First the deviation and diplopia in the primary position and primary and secondary deviation are determined. Tests are made to determine the diplopia and deviation in different directions of gaze. Homonymous diplopia, whether large or small, which increases as the eyes are carried to the right indicates underaction of some muscle of the right eye or overaction of some muscle of the left. A crossed diplopia, which increases as the eyes are carried to the right, indicates underaction of some muscle of the left eye or overaction of some muscle of the right eye. Accessory tests for confirmation of the diagnosis are: determination of the limitation of monocular movement; the pointing or projection test, and torsion tests. Diagnosis is individual in usual and in unusual cases; diagnosis in cases of slight paralysis and in complex cases (especially the complexities caused by spasm of the associate or antagonist muscles) is discussed in each instance as a separate item.

It will always be a regret to the ophthalmologic world, and a tremendous loss to it as well, that Dr. Duane was not able to complete this work on the ocular muscles.

SPAETH, Philadelphia.

VASCULAR NOISES IN THE EAR. L. BALDENWECK, Rev. d'oto-neuro-opht. **12**:81 (Feb.) 1934.

After a review of the anatomy and physiology of the circulation and vasomotor innervation of the ears Baldenweck discusses exhaustively both physiologic and pathologic noises in the ear. The normal sounds of the circulating blood may be

perceived by a person under conditions of perfect silence, as in a sound-proof chamber. The least extraneous noise causes their disappearance. These noises are described as a beating sound at first, which is soon replaced by a buzzing. The source is the movement of the blood in the vessels. In certain pathologic conditions, notably obstruction of the eustachian tube or of the external auditory meatus, they may be perceived outside the sound-proof chamber.

Discussion of abnormal vascular noises is limited to those produced by (*a*) modification of the blood mass, (*b*) lesions of the labyrinthine vessels, (*c*) disturbances of the vasomotor sympathetic system and (*d*) lesions of the extra-auricular vessels. The first two causes are represented in modifications of tension (as in anemia and severe hemorrhage), anemia and congestion, arteriosclerosis and angiospasm of the labyrinthine vessels and otosclerosis. Noises produced by disturbances of the vasomotor sympathetic system are discussed at length. The roaring noises observed after the ingestion of quinine and sodium salicylate in dyspepsia and in hepatic diseases are caused by vasodilatation. In patients with exophthalmic goiter, women at the menopause and those with pelvic diseases, endocrine disturbances together with vasosympathetic dystonia come into play. Instability of the vasomotor system accompanying neuroses may easily react on the labyrinth and produce tinnitus. The same is true in patients with migraine and with the aura of epilepsy. Tinnitus following cranial trauma arises from modifications of the pressure of the cerebrospinal fluid and from meningeal adhesions, but it seems logical to presuppose a derangement of the sympathetic fibers surrounding the cerebral vessels which affects the vascular supply of the labyrinth or of the auditory nuclei. A curious phenomenon is tinnitus produced by pressure either on the head or neck or even, as in a case seen by Bourgeois, on remote parts of the body. A special lability of the vasomotor system must be assumed in such cases. Other cases that are similar but in which there is some pathologic condition of the ear or of the vessels supplying it have been observed. Probably, here, special connections between the skin and the deep sensibilities and the circulation of the ear exist. Another group of cases in which the noises are of sympathetic origin occurs in patients with hyperthyroidism and hypertension and in those undergoing the menopause; Jones and Knudsen include also cases in persons with foci of infection in the teeth, tonsils and sinuses. In some of these cases, compression of the vessels of the neck or certain positions of the head cause disappearance of the noises. Baldenweck thinks that this is due not to suppression of the blood flow but to an effect produced on the sympathetic plexus surrounding the vertebral artery, for it is not possible to influence the circulation in the internal auditory artery by such a procedure, since it arises from the circle of Willis.

Vascular noises in lesions of the extra-auricular vessels are noted in cases of aneurysm of the neck, head and interior of the skull, pulsating exophthalmos and intracranial tumors.

In the vasomotor type the therapeutic indications are such measures as tend to correct the vasodilatation or constriction: epinephrine, acetylcholine, physostigmine, jaborandi and atropine. Often the whole list must be used in turn. Other useful remedies are the administration of bromides, phenobarbital and cimicifuga, the application of leeches to the mastoid area and bloodletting. Surgical measures include rupture of peritubal adhesions, intranasal operation, lumbar puncture, sympathectomy of the perivertebral plexus and ligation of the large vessels in cases of intracranial aneurysm. Section of the auditory nerve is not recommended.

DENNIS, San Diego, Calif.

THE CONTRIBUTION OF PHYSICAL ILLNESS TO THE DEVELOPMENT OF BEHAVIOR DISORDERS IN CHILDREN. LEO KANNER and SANDER E. LACHMAN, Ment. Hyg. **17**:605 (Oct.) 1933.

Behavior problems may arise in otherwise normal children as a result of a complex of factors associated with non-neurologic physical illnesses. The authors have excluded from their series children suffering from developmental defects,

feeblemindedness, juvenile dementia paralytica, encephalitis, birth injuries and other organic disorders of the endocrine or nervous systems. The patients are divided into two groups, those with a previously stable personality and those with personality instabilities preceding the physical illness. Most children, of course, fall into neither category. In fact, in the majority of children bodily ailments produce no permanent or extensive change in the established behavior patterns. As an instance, however, of a behavior disorder precipitated by a physical illness, the authors cite the case of a girl, aged 12, with an intelligence quotient of 117. Following a serious attack of bronchopneumonia she became the center of attention. Oversolicitous about her health, the family constantly referred to illness, poured tonics into her and subordinated the household routine to her whim, on the grounds of supposed delicacy or sickliness in the child. She could enslave her parents by a cough and wheedle favors from school teachers by a complaint of pain.

Sometimes neglect or resentment on the part of the parents, rather than oversolicitousness, is the significant factor. The case of a boy, aged 9, with an intelligence quotient of 115, is described. He suffered from asthma due to a real allergy to bed feathers. The parents found the illness and the consequent inconveniences and financial drain very uncomfortable and sent the child to a sympathetic grandmother in the country. With her he made an excellent temperamental adjustment in spite of the dyspneic spells. On her death he was returned to his parents, who stigmatized the asthmatic seizures as wilful and a stubborn habit. He was subjected to nagging and his life was made miserable. Tantrums and disobedience developed, and the boy was referred for psychiatric study as a "problem child."

Another instance of a personality problem associated with asthma is cited to illustrate the aggravation of a preexistent behavior disorder by physical illness. In this case the child had genuine asthmatic seizures; learning that these were followed by the granting of special favors he began to produce spurious attacks to enforce all sorts of unreasonable requests. The parents, unable to distinguish the two types of dyspneic episodes, soon became enslaved to his whims.

The authors warn against hasty or dogmatic assumptions about the mechanisms of these behavior problems. No single explanation—such as parental inadequacy, infantile sexuality or a feeling of inferiority—will cover all cases. Among the modifying factors peculiar to each case are the previous personality of the patient, the attitudes of the parents, physicians and siblings, the nature of the illness and a variety of incidental social factors. Primary attention must be paid to remedying the physical illness, but the therapy must not be disproportionate. Undesirable parental attitudes must be evaluated and corrected, and the gains derived from the continuation of the behavior disorders must be reduced.

DAVIDSON, Newark, N. J.

STATISTICAL STUDIES IN 120 CASES OF FACIAL PALSY. KIYOJI KUBO and NOBUYUKI HIKARU, Folia psychiat. & neurol. japon. **1**:18 (Dec.) 1933.

Kubo and Hikaru present the results of a statistical study of 120 cases of facial palsy observed during 1928 to 1932; 65.8 per cent of the cases were in men and 42.2 per cent in women. The ages of the men ranged from 35 to 45 and those of the women from 26 to 35. Facial palsy seemed to occur more frequently during June, July and August. In only two instances was there a history of the occurrence of facial palsy in the family of the patient. Recurrences were observed in ten cases. As to the etiologic possibilities, a "rheumatic" origin (slight cold or no traceable cause) was noted in 65.9 per cent of the cases and an otogenic origin in 10 per cent, while in 16.7 per cent palsy occurred following infectious diseases. Influenza was considered as an etiologic factor in 3.3 per cent, parotitis in 2.5 and angina in 3.3 per cent. In 1.7 per cent facial palsy occurred during the puerperium; in 3.3 per cent, after fever (in children), and in 0.8 per cent, after injection of typhoid vaccine. Traumatic palsy caused by surgical intervention was observed in 4.2 per cent. In 9.2 per cent of the cases the Wassermann reac-

tion was positive. Prodromal symptoms were absent in 45.8 per cent; pain, hyperesthesia and tumescence were recorded in 10.8 per cent; occipital or cervical pain in 10 per cent; earache in 9.2 per cent; tinnitus in 6.7 per cent; twitchings of the eyelids with lacrimation in 7.5 per cent; headaches in 5 per cent, and fever in 3.3 per cent. No history of prodromal signs was obtained in the remaining 21.6 per cent of the cases. In 93.3 per cent the palsy was of peripheral and in 2.5 per cent of central origin. In 47.3 per cent it was on the right side and in 52.7 per cent on the left. Bilateral palsy was not observed. A complete reaction of degeneration was present in 12.5 per cent, incomplete in 13.3 and good electrical response in 65.8 per cent, while in the remaining 8.4 per cent no electrical reactions were recorded. In 13.8 per cent there was disturbance of taste, salivation and hearing; in 10 per cent there was disturbance of taste and salivation; in 8.5 per cent there was disturbance of lacrimation, salivation and hearing; in 58.9 per cent there were no sensory or secretory changes, and for the remaining 8.5 per cent no data are available. In four cases the phenomenon of *Krokodiltränen* (crocodile tears) was observed. Contracture was present in five cases. The authors believe that electrotherapy is the most efficacious form of treatment. They do not advise, however, the immediate application of electrotherapy, as it often aggravates pain and may even increase the palsy. In instances of a mild reaction of degeneration they recommend weak cathodic galvanization for from five to ten minutes; in cases without reaction of degeneration, moderate faradization. They warn against excessive faradization, especially in advanced cases, as it frequently causes contractures. They supplement electrotherapy with training in facial expression, making the patients articulate words before a mirror and if necessary help the facial muscles with the hands. They strongly recommend cessation of electrotherapy at the first sign of a threatening contracture. The authors report complete recovery in 40.9 per cent of cases and slight improvement in 25.5; they offer no definite data for the rest of the group.

NOTKIN, Poughkeepsie, N. Y.

THE ANAPHYLACTIC BASIS OF RHEUMATISM. C. E. JENKINS, Brit. M. J. **1**: 186 (Feb. 3) 1934.

Jenkins attempts to survey the possible connection between rheumatism and anaphylaxis. On the basis of cutaneous tests there is a fairly good argument that most patients are allergic to the streptococci. There is no satisfactory evidence that a specific organism is responsible. Jenkins' contention is that if the description of the general and prodromal features of arthritis deformans as given by the Arthritis Committee and by various standard textbooks is compared with the description of serum sickness by Kolmer, Muir and Ritchie, Zinsser, and others, it will be found that the two are interchangeable. Reviewing various work that has been done on anaphylaxis, a number of important findings tend to explain some of the reactions in arthritis. For example, repeated injection of antigen into an anaphylactic animal gives rise to increasingly severe local reactions; thus any damage done by streptococci or their toxins during the early stage of infection may leave the damaged area open to attack by the circulating antigen. Injury to the skin of a sensitized animal when antigen is in the circulation may produce a local allergic reaction due to the actual excretion of the antigen into the injured area. It can be inferred from this that once a joint is damaged a more or less continuous irritation is set up by the antigen in the blood and a vicious circle is started which can be broken only by removal or neutralization of the circulating antigen. Also, once the anaphylactic reaction has been established there is nothing to prevent any organism from causing the disease, provided it is capable of producing allergy in man, and this may explain why cases are reported from time to time as being due to some bacterium not usually associated with the disease.

The liability to allergy in general is a weakness of the host, inherited or acquired; that the actual allergic state to some particular substance is itself truly transmitted is doubtful. Transmission through the mother has been recorded

frequently, but this is probably due to the passage of antigen through the placenta. A hereditary liability to anaphylaxis has been found in animals, and the adduced facts may explain why rheumatism is frequently a familial disease and may also constitute an answer to the triumphant query why, if pyorrhea is a cause of rheumatism, every sufferer from the former disease does not also exhibit evidence of the latter.

Two methods of desensitization are discussed. Nonspecific desensitization has been induced by many substances, ranging from sodium chloride to proteins, and if these various substances were tried in man a number of cures would occur. Specific desensitization consists of feeding the animal the antigen that caused the condition. A certain number of drugs have long been known as depressants of anaphylactic shock. Among these are salicylates, acetylsalicylic acid, phenyl salicylate, antipyrine, some narcotics and anesthetics, calcium, magnesium, bromides, iodides and some resins. None have any influence on the anaphylactic state itself.

FERGUSON, Niagara Falls, N. Y.

TWELVE CASES OF BINASAL CONTRACTION OF THE VISUAL FIELD OCCURRING IN INTRACRANIAL DISEASE. C. VINCENT and E. HARTMANN, Ann. d'ocul. **171**:193 (March) 1934.

Vincent and Hartmann report twelve cases of binasal contraction of the visual field in intracranial disease. The rarity of primary atrophy of the optic nerve (two cases) and the incidence of choked disk (eight cases) make them believe that choked disk or factors that cause choked disk (cerebrospinal hypertension?) play an important rôle in binasal hemianopia. This belief was confirmed by two cases of tumor of the parietal lobe. In the other cases it was thought probable that direct lesions of the optic nerve tracts in the region of the chiasm were a factor. This opinion resulted from the observation of a few cases in which there was no choked disk or only a slight edema superimposed on primary atrophy of the optic nerve. On the other hand, one should remember that the great majority (seven of nine cases) of the verified lesions were situated in the region of the optic chiasm (arachnoiditis in four cases) or not far from the optic chiasm (meningioma of the lesser wing of the sphenoid in three cases).

It is probable that the mechanism varies. In certain cases binasal hemianopia is produced by direct action of the primary lesion (tumor or arachnoiditis); in others it is caused by a distant disturbance and a different mechanism. In the first group the authors were able to differentiate between compressions by bands caused by arachnoiditis and by vascular bands (Temple Fay and Grant). In the second group, the changes in the visual fields were associated with remote tumors and choked disk.

It is a question whether choked disk alone can produce changes that are more marked in the nasal halves of the visual fields. The authors believe that edema of the optic nerves and papillas, hypertension of the fluid in the sheaths of the optic nerves and retardation of the ocular circulation may disturb the normal function of the visual fibers. The temporal retinal fibers may be more easily affected because they are more delicate. This seems to be true in certain disturbances of retinal circulation.

It seems proper to point out that glaucoma usually affects the nasal visual field as does atrophy of the optic nerve with excavation but without ocular hypertension, in which retinal anemia may play an important rôle through arteriosclerosis; and in visual disorders after loss of blood binasal hemianopia may be observed. One of the authors has reported two cases; Traquair has reported another case, and several others have been reported by Lelièvre. In amblyopia due to quinine the nasal visual field is, at times, difficult to improve. In all these diseases, no satisfactory explanation has been given for the predominance of nasal contraction of the visual field. Vincent and Hartmann believe that there is a possibility that the temporal retinal nerve fibers are more delicate than the nasal fibers.

BERENS, New York.

CLINICAL STUDIES OF MENTAL TESTS. SIMON TULCHIN, Am. J. Psychiat. **13**: 1237 (May) 1934.

To accept the score of psychometric tests at its face value without effort to interpret it in the light of other data is to open the way to the possibility of serious error. In interpreting the intelligence quotient, several sets of factors must be evaluated. These include: (1) the physical, linguistic, economic, social and cultural status of the subject, as well as his emotional attitude and cooperation during the test, (2) chronological age and training factors; (3) comparison with other psychologic tests, and (4) criteria of intelligence based on data other than psychometric tests.

Tulchin points out that the chance of obtaining a very high intelligence quotient falls as a person grows older, so that as between two equally bright siblings, the elder (if both have a high intelligence quotient) is likely to have a lower quotient. The possibility that certain special training has been given to younger subjects, resulting in superior skill at the lower mental age levels, must also be appraised. As an instance of the misinterpretation of a test score, the author cites the following case: A boy, aged 14, suffered from shyness, speech difficulties and lack of sociability. The intelligence quotient was reported as 51, and the recommendation accompanying this score suggested placement in an ungraded school. Further study showed, however, nerve deafness of 60 per cent and an intelligence quotient on a nonlanguage test of 86. With performance tests the boy received a superior score. Had the first recommendation (to place him in an ungraded school) been followed, serious consequences might have resulted.

The author also reports an analysis of 109 reexaminations to determine the shift in the intelligence quotient. The interval between examinations averaged twenty-one months. The average shift in intelligence quotient (regardless of direction) was 9 points. In only 12 per cent of the cases did it vary more than 15 points. The group with the lowest intelligence quotients (below 85) showed the least change—an average of 7.7 points—while the group with the highest quotients (over 115) showed the greatest change—an average of 10.4 points. The children with good cooperation showed the least change—in 81 per cent of the cases in this group the change was less than 5 points. Among those with poor cooperation, only 40 per cent showed a variation of less than 5 points. The greatest variation occurred in the group with special handicaps, in which only 21 per cent showed a shift of less than 5 points.

Tulchin concludes by stressing that the psychologist must know how to integrate his findings with the data secured by social workers, educators and psychiatrists.

DAVIDSON, Newark, N. J.

DISTRIBUTION OF NEUROGLIA IN THE SPINAL CORD OF MAN AND OF ANIMALS. T. KAMIMURA, Folia psychiat. & neurol. japon. **1**:87 (Dec.) 1933.

Kamimura studied the glial elements in the phylogenetic animal scale. He found that the ependymal cells are better developed the lower the animal is in the scale of the vertebrates. In the lower animals there are well developed macroglia cells. In fishes and in reptiles one sees macroglia cells in various stages of development. In birds, mammals and man one finds the astrocytes. Occasionally one sees this element in cyclostomes and also in fishes. Only beginning with reptiles does one find protoplasmic macroglia cells in the gray substance. These cells are poorly differentiated, however, in reptiles. The spinal cord of adult vertebrates contains completely developed forms of microglia and oligodendroglia cells. In the lowest young vertebrates one finds young microblasts and oligodendroglioblasts. The microglia cells are numerous in man, mammals, birds and cyclostomes and especially in fishes, but less numerous in reptiles and amphibians. Generally they are more numerous in the gray substance than in the white; only in fishes and cyclostomes are they equally distributed in the gray and in the white matter.

The microglia cells show phylogenetically a close relationship to the pia and to the blood vessels. They multiply by the method of amitotic division of the nucleus, the typical figures of which are occasionally seen in the adult cord. The form and size of the microglia cells are characteristic for the type of animal. In the more highly developed animals the microglia cell has always an unusual complicated system of processes. In man and in mammals one finds most frequently cells with an oval or round nucleus.

In the lowest vertebrates the oligodendroglia cells are scarce in the spinal cord and seldom show the tendency to group or line formation. They are more numerous in the gray matter of the spinal cord than in the gray matter of the cerebrum and cerebellum. They are particularly rich in number around the central canal. One finds large masses of microglia and oligodendroglia cells in the substantia gelatinosa Rolandi.

One never sees the mitotic figures of the oligodendroglia cells in the spinal cord of the adult vertebrate. The oligodendroglia cells are better developed in the white substance than in the gray substance. They resemble sometimes the macroglial element when located around the vessels in the white substance. Generally, the oligodendroglia cells are round or oval bodies and show no particular characteristic for a given species. They are always small in lower animals, especially in fishes and in cyclostomes. Kamimura believes that microglia cells are of mesodermal origin.

NOTKIN, Poughkeepsie, N. Y.

A SIMPLE METHOD OF PRODUCING VASODILATATION IN THE LOWER EXTREMITIES. EUGENE M. LANDIS and JOHN H. GIBBON JR., Arch. Int. Med. **52**:785 (Nov.) 1933.

Vasodilatation of the vessels of the lower extremities can be obtained by immersing the forearms and hands in warm water. With normal blood flow in the legs and feet, the temperature of the toes should rise to or above 31.5 C. (88.7 F.) within one-half hour if the forearms are immersed in water at 45 C. The surface temperature of the toes is determined thermo-electrically, the thermal junctions being placed in contact with the skin on the dorsal surface of the distal phalanx of the toe just proximal to the base of the nail. The thermal junction may be covered with a single layer of adhesive plaster if desired. When the skin temperature (of the toes) reaches 26 C. (78.8 F.) or less, the hands and forearms are immersed in a water bath at 45 C. The temperature of this water bath is maintained at between 43 and 45 C. The skin temperature (of the toes) is read every minute for thirty-five minutes unless a temperature of 32 C. (89.6 F.) is reached sooner. The results are indicated in twenty-four patients. Group 1 consisted of seven patients, all showing normal response; two had phlebitis and two sciatica; the others had an old embolism, an arteriovenous fistula and arthritis, respectively. The lowest temperature at the toes was 32.2 C. (90 F.). The maximum time required in this group for the temperature to reach 32 C. was twenty-two minutes. These responses are considered normal. Group 2 consisted of five patients with thrombo-angiitis obliterans. In none of the group did the skin temperature of the affected leg rise above 25.6 C. (77.8 F.) within thirty-five minutes. The average temperature after the period of immersion was only 22 C. (71.6 F.). This indicates seriously inadequate response. Group 3 was made up of seven patients with arteriosclerosis. In three of these the norm of 32 C. was reached or exceeded; in six the norm was not reached. In these six the highest temperature reached was 30.5 C. (86.9 F.); the lowest, 19.3 C. (66.7 F.). Group 4 consisted of three patients with acrocyanosis. Exact figures are not given, but in all three patients the more involved lower extremity failed to show a vasodilator response.

Because the best results in the treatment of peripheral vascular disease by sympathetic gangliectomy can be obtained only if the vessels retain some ability to dilate, this technic is considered especially valuable in determining the surgical

prognosis in these cases. The method is simple, and requires no apparatus except the thermo-electric couple and a simple enamel arm bath for immersing the forearms. The method is devoid of any danger.

DAVIDSON, Newark, N. J.

OPTIC NEUROMYELITIS. RICHARD A. PERRITT, Arch. Ophth. **11**:492 (March) 1934.

Optic neuromyelitis is a rare disease, only a few over fifty cases being cited in the literature, five of which are recorded in English. The first anatomic-pathologic description of the condition was given in 1889 by Achard and Guineau, although a few cases were reported previously by other authors. Devich, in 1894, gave the disease its name; other cases were afterward published by Katz, Brissaud and Rochon-Duvigneaud and by Hilion, who in his thesis reported forty-five cases. Complete histopathologic examinations were recorded in sixteen of the twenty-four fatal cases. Later came the observation of Hoffman, Cobledick, Miashita, Goulden, Holden, Jendralski, Dolffus, Strumpell, Dreschfeld, Raverdino, van Gehuchten, Bouchut, Dechanne and Bogaert. A good recent summary of the subject is that of Salvati. Perritt has included a report of two additional cases.

Clinically, the disease is one of acute bilateral optic neuritis which is followed in a variable length of time by myelitis. Occasionally the ophthalmoscope does not help directly, because, as was true in one of these cases, only the signs of retrobulbar neuritis are present. Ocular movements and pressure on the bulb may elicit severe pain, but this phenomenon is also sometimes observed in retrobulbar neuritis due to other causes. The neuritis may be followed by complete blindness or only impairment of vision, with restriction of the visual field for white and for colors and occasionally with central scotomas. Return of vision is always slow but occurs in about 50 per cent of the cases.

The neurologic signs and symptoms of myelitis are naturally present. Other general symptoms may be found, but they are not as common. The etiology is still obscure. The hypothesis has been advanced that there may be a vasomotor action exerted by a disease of the gray matter of the optic nerve and by a destruction of the trophic centers of these nerves to cause the progressive myelitis. In 50 per cent of the reported cases the patient recovered, and in all vision returned to normal or to nearly normal. The other cases terminated in death. The course is usually acute.

Perritt calls attention to the differences which exist in this condition as compared with multiple sclerosis when associated with retrobulbar neuritis. The latter has a chronic course, and while the visual defects may come on acutely and subside rapidly the disease is prone to recur and to leave permanent damage.

SPAETH, Philadelphia.

LOCALIZATION OF CONSCIOUSNESS AND EMOTION. LELAND B. ALFORD, Am. J. Psychiat. **12**:789 (Jan.) 1933.

In an effort to determine the cerebral localization of the functions of consciousness and emotion, Alford has observed the effects on these functions of lesions in various parts of the brain. Consciousness is evaluated in terms of awareness, allowance being made for the uncertainty and inattention natural in any case of disease of the brain. In thirty-three right-handed persons with left hemiplegia, no case of confusion was noted. This appears to exclude the right basal region from any participation in the function of consciousness. The lobar extirpations of Dandy are cited as evidence that no other part of the right cerebral hemisphere (in a right-handed person) can be concerned with consciousness, since these extirpations were not followed by any significant defect in this function. Involvements of the speech zone of Head were often associated with aphasia but not with loss of awareness, nor were any instances of serious defect in consciousness found in the early stages of tumor of any of the left cerebral lobes. In this manner, all parts of the cerebrum except the left base were eliminated. In a series of fifty-five capsular lesions in the left hemisphere confusion was noted twenty-seven times.

This suggests, both by elimination and by direct clinical evidence, that consciousness is served by an area somewhere at the left base. Examination for emotional reactions resulted in a similar limitation of sites to the left base. This is corroborated by the frequency of emotional disturbances in postencephalitic persons, although in view of the primitive nature of the basal ganglia there is no theoretical reason why there should be any functional lateralization in this area. In spite of the identity of the general site of these two functions, Alford is inclined to consider them separate psychic entities. He suggests that further research for pathologic changes in the psychoses give adequate attention to the basal areas instead of limiting itself to the cortex as heretofore.

DAVIDSON, Newark, N. J.

EXAMINATION OF THE CEREBROSPINAL FLUID IN CASES OF RETROBULBAR NEURITIS. POPEK, Ann. d'ocul. **170**:610 (July) 1933.

Popek emphasizes the necessity of examining the cerebrospinal fluid in cases of retrobulbar and intra-ocular neuritis, which are often caused by multiple sclerosis (according to some authorities, in from 55 to 70 per cent of cases). In one third of the cases of multiple sclerosis the involvement of the optic nerve is the first clinical symptom; others appear sometimes years later. According to Popek's experiments, at a time when neurologic examinations give absolutely negative results examinations of the cerebrospinal fluid reveal that multiple sclerosis is the cause of the optic neuritis. Among twenty-one patients suffering from retrobulbar or intra-ocular neuritis there were eleven (52.4 per cent) who showed the characteristic signs of multiple sclerosis in the cerebrospinal fluid: (1) a normal or slightly increased quantity of albumin without pleocytosis or with very slight pleocytosis and (2) strongly positive colloidal gold reactions with a negative Wassermann reaction of the cerebrospinal fluid and of the blood (serologic colloid dissociation). Symptoms of multiple sclerosis were found in only one patient; three other patients complained of only a few isolated neurologic symptoms and also felt perfectly well. In the anamnesis, two other patients complained of symptoms characteristic of multiple sclerosis, but at the time when they had retrobulbar neuritis they had had no symptoms or signs of multiple sclerosis. As to the five other patients, neither anamnesis nor detailed examination revealed symptoms or signs of nervous disease, in spite of the signs in the cerebrospinal fluid suggestive of multiple sclerosis. Three months later, the first patient showed symptoms characteristic of multiple sclerosis, while the others have had no disturbance. The duration of the observation varied from nine to twenty-eight months.

BERENS, New York.

GENERALIZED THROMBO-ANGIITIS OBLITERANS. WALTER BIRNBAUM, MYRON PRINZMETAL and CHARLES L. CONNOR, Arch. Int. Med. **53**:410 (March) 1934.

Although still few in number, reports of thrombo-angiitis obliterans affecting vascular areas other than the extremities are accumulating. The disease is seldom thought of as generalized, and its manifestations are probably often overlooked. A case of thrombo-angiitis obliterans affecting the vessels of most of the viscera is here reported. The patient, a youth aged 19, had an unimportant past and family history. He smoked from twenty to thirty cigarets daily. His race is not stated. His complaints included: painful swelling of the legs, nausea, vomiting, abdominal pain, dimness of vision, fever, jaundice and hemoptysis. Ophthalmoscopy showed that the retinal arteries were tortuous, dilated and streaked, while the veins of the fundus were similarly affected. The blood pressure was 120 systolic and 70 diastolic. The hemoglobin content was 54 per cent, and Wassermann tests and blood cultures gave negative results. In the hospital there developed thrombosis of an antecubital vein and meningeal signs which were not explained by the results of examination of the spinal fluid. The patient died in coma three weeks after admission to the hospital. Postmortem examination showed that the left suprarenal gland was enlarged to three times its normal size. Only a shell of supra-

renal cortex remained, but the medulla was destroyed and replaced by a firm, extensive hemorrhagic clot. The saphenous vein was thickened and contained an antemortem thrombus. The smaller arteries throughout the body were thickened, and many of them contained thrombi. Almost all the visceral vessels were involved in this process. The adventitia showed an increased amount of connective tissue, while the intima was the site of a proliferative process encroaching on and narrowing the lumen. No attempt at the formation of a collateral circulation through the vasa vasorum was noted. From the clinical standpoint, the changes in the retinal vessels are considered of great importance, since these, being the only visible vessels, offer a clue to the diagnosis. DAVIDSON, Newark, N. J.

COLOR VISION AND ITS ANOMALIES. A. POLACK, Ann. d'ocul. **171**:289 (April) 1934.

Polack points out that the study of color vision and its anomalies is still handicapped by certain theories which should be disregarded. A more extensive investigation should be made of the theories which oppose these obstacles to the study of the normal evolution of color vision. Young believed that the number of shades which the normal eye could differentiate in the spectrum could not be estimated, whereas Polack believes that the number of shades is not higher than one hundred and fifty. The trichromatic theory, based on Young's supposition, does not agree with the known facts concerning color vision. Color vision cannot be reduced to three fundamental colors, and therefore the terminology derived from Young's theory should be replaced.

The physiology of color sense is characterized by two outstanding factors: the position of maximum illumination or curve of illumination in the spectrum and the presence of two unitonal areas, one in the red and the other in the violet. In anomalies of color vision the first factor or both may be modified.

When displacement of maximum luninosity without extension of the unitonal areas occurs, the Rayleigh type of color anomaly is present. When there is displacement of maximum luminosity with extension of the unitonal areas, color blindness of the Nagel type is observed if displacement is toward the red and color blindness of the Dalton type if the displacement is toward the violet. Total achromatopsia is present when displacement of the unitonal area toward the violet is still more accentuated and the two unitonal areas are fused extending over the visible spectrum. BERENS, New York.

MONOSODIUM THYROXINE, DESICCATED THYROID AND AN IMPURE SODIUM SALT OF THYROXINE: COMPARISON OF THEIR EFFECTS WHEN ADMINISTERED ORALLY WITH THE EFFECT OF THYROXINE INJECTED INTRAVENOUSLY IN ALKALINE SOLUTION. WILLARD O. THOMPSON, PHEBE K. THOMPSON and LOIS F. N. DICKIE, Arch. Int. Med. **52**:576 (Oct.) 1933.

The purpose of the study here reported was to determine the effectiveness of the oral administration of thyroxine and to compare this with the effectiveness of its administration by parenteral routes. Six myxedematous patients were studied, and the results were calculated on the basis of the daily dose adequate to maintain basal metabolism at normal level. Expressed as milligrams of iodine content of the daily dose, the results in one patient were: desiccated thyroid by mouth, 0.19; crystalline thyroxine intravenously, 0.2; impure sodium salt of thyroxine by mouth, 0.46, and monosodium salt of synthetic thyroxine by mouth, 0.85. Expressed in actual raw dosage, the amounts required daily by the same patient were: 0.3 mg. of crystalline thyroxine intravenously; 1.25 grains (81 mg.) of desiccated thyroid by mouth; 1.3 mg. of the monosodium salt of thyroxine by mouth, and 0.7 mg. of impure sodium salt of thyroxine orally. The parenteral route thus appears to be the most effective for thyroxine; and even this would, on the basis of actual iodine content, appear to be slightly less effective than desiccated thyroid orally. When given by mouth the synthetic thyroxine seems to be less effective than

the impure sodium salt. (Similar results were obtained in all six cases.) One explanation is probably that there are variations in absorption of these preparations from the gastro-intestinal tract due to differences in their solubility.

DAVIDSON, Newark, N. J.

A CEREBELLAR TUMOR IN THE REGION OF THE VERMIS, DIAGNOSED BY VESTIBULAR EXAMINATION. J. BARBIER and R. MAYOUX, Rev. d'oto-neuro-opht. **11**:518 (July-Aug.) 1933.

The patient suffered with slight equilibrial disturbances, frontal headache and vertigo. The eyes were normal. The tension of the spinal fluid was 29 (Claude); the Queckenstedt sign was negative; the fluid contained albumin, 0.2 and 2 cells per cubic millimeter, and the Bordet-Wassermann test was negative. Neurologic examination revealed only disturbed gait while walking with the eyes closed. Vestibular examination showed bilateral, spontaneous, horizontal nystagmus, a tendency to fall backward, which was not influenced by the caloric test, normal excitability of the horizontal canals and inexcitability of the vertical canals. Operation revealed a cystic glioma of the right cerebellar hemisphere near the median line. The interest of the case lies in the paucity of neurologic findings and the precision of the labyrinthine signs. The bilateral and symmetrical inexcitability of the vertical canals, together with the absence of modification of falling by cold irrigation, in a patient with disturbance of equilibrium and good hearing warranted the diagnosis of a tumor of the cerebellum in the region of the vermis. Wishart showed that median cerebellar tumors caused symmetrical vestibular disturbances, and Bárány proved that in these cases the direction of falling was not modified by vestibular stimulation or the position of the head.

DENNIS, San Diego, Calif.

COMPARISON OF NEOARSPHENAMINE AND ARSPHENAMINE. J. P. THORNLEY, Arch. Dermat. & Syph. **27**:185 (Feb.) 1933.

In a study of 999 patients with syphilis, Thornley finds little difference in therapeutic efficacy between arsphenamine and neoarsphenamine. The percentage figures for the former were: cured, 24 per cent; probation, 22; relapse or serologic resistance, 31, and improved, 22 per cent. With neoarsphenamine the figures were: 26, 28, 22 and 23 per cent, respectively. This shows little difference between the two drugs, with a slight bias in favor of neoarsphenamine. A study of untoward reactions was also made: the incidence in the arsphenamine series was 8 per cent slight and 7 per cent severe reactions, while of the patients receiving neoarsphenamine, 5 per cent showed slight and 4 per cent severe reactions. This estimate of unfavorable reactions following the use of neoarsphenamine, 9 per cent, differs widely from the commonly reported figure, Thornley's results being much better than those reported by other clinics. His explanation is that "it is because I have never permitted a single dose of neoarsphenamine, silver arsphenamine, or arsphenamine to be given in concentration by a syringe. Neoarsphenamine and arsphenamine are given in exactly the same dilution and dose and by the gravity method." In view of the infrequency of reactions by the gravity method, the author strongly urges the adoption of this technic. His concluding warning is: "As long as physicians insist on giving neoarsphenamine with a syringe, they are looking for trouble, and they will certainly find it."

DAVIDSON, Newark, N. J.

THE GREAT VEIN OF GALEN AND THE SYNDROME OF INCREASED INTRACRANIAL PRESSURE. T. H. B. BEDFORD, Brain **57**:1 (March) 1934.

The authenticity of the two cases of hydrocephalus that Dandy considered as being caused by obstruction of the great vein of Galen is open to question. In order to verify Dandy and Blackfan's statement that hydrocephalus occurs when the great vein of Galen is obstructed near its origin (based on one positive result

in ten dogs on which operation was performed) Bedford, following in the main the technic of the aforementioned author, obstructed this vein at various points along its course in forty-seven animals. In none of these did hydrocephalus develop. Only twenty-eight animals lived for at least three months, when they were killed. The arrangement and communications of the veins of the velum interpositum of the dog are described, and they are not identical with those in man. For the presence of collateral circulation, the great vein of Galen can be occluded at the following locations: (1) in the anterior part of its course, (2) at the point where it is joined by the basilar veins and (3) in the posterior part of its course.

The experiments tend to show that hydrocephalus does not develop after occlusion of the great vein of Galen. The positive finding of Dandy and Blackfan and of Guleke was probably due to some entirely different cause, perhaps meningoencephalitis. Stopford's theory is reviewed, and according to Bedford it is lacking in fact and is based on indirect evidence.

MICHAELS, Boston.

THE IRON REACTION IN PARETIC NEUROSYPHILIS. H. HOUSTON MERRITT, MERRIL MOORE and H. C. SOLOMON, Am. J. Syph. **17**:387 (July) 1933.

Excess iron is found in the brain in two general types of disease: hemorrhages and dementia paralytica. In the former, the iron is a residue of broken-down blood cells and lies free in necrotic tissues or in perivascular spaces. In cases of dementia paralytica, spicules of iron, characteristically stained by the Turnbull blue technic, are found in the walls of the vessels and the microglia cells. An absolute diagnosis of dementia paralytica can be made at autopsy in a few minutes by the Spatz method. A small piece of brain tissue removed from the cortex or corpus striatum is rinsed in physiologic solution of sodium chloride and allowed to stand for fifteen minutes in a concentrated solution of ammonium sulphide. It is then rinsed again and pressed down on a slide. In cases of dementia paralytica the iron pigment stands out clearly in the walls of the blood vessels as black dots and globules. A similar finding has been reported in cases of trypanosomiasis, but not in any other organic disease of the nervous system. In instances of hemorrhage into the brain, the iron is found in circumscribed areas. In neurosyphilis other than dementia paralytica, deposits of iron are not usually found. The Spatz reaction is weak or absent in slowly developing, stationary cases, and in autopsies in the cases of patients who died of intercurrent disease during a remission. No adequate explanation of the source of the iron has been advanced.

DAVIDSON, Newark, N. J.

RARE CASES OF OCULAR SYNKINESIS. H. COPPEZ, Rev. d'oto-neuro-opht. **11**: 503 (July-Aug.) 1933.

This article supplements the author's previous observations (*Rev. d'oto-neuro-opht.* **10**:12 [Jan.] 1932) by the description of two additional cases: the syndrome of Marin Amat and synkinesis between the frontal and the external rectus muscles. The former was the case of a young girl who had recovered from an attack of Bell's palsy on the right side. When she smiled the right orbicularis muscle contracted and closed the eye, a facial synkinesis of the buccopalpebral type. When she chewed, the palpebral orbicularis muscle contracted synchronously with the movements of mastication, synkinesis between the fibers of the facial and the motor branch of the fifth nerve. There was no excess salivary or lacrimal secretion. The synkinesis is assumed to be central, with irradiations at the level of the motor nuclei. The second case was that of a young man with permanent convergent strabismus of the left eye, in which a tenotomy of the left internal rectus muscle had been done. When he looked to the left, the left brow was raised and remained in this position while he looked downward and to the left. When the eye was moved from abduction to adduction the brow assumed a normal position when the eye reached the midline, and remained there during further

adduction. The seat of the synkinesis is central; fibers pass from the sixth pair into the seventh at the knee of the facial nucleus.

DENNIS, San Diego, Calif.

INFLUENCE OF SODIUM NITRITE ON THE CARDIOVASCULAR SYSTEM AND ON RENAL ACTIVITY. SOMA WEISS and LAURENCE B. ELLIS, Arch. Int. Med. **52**:105 (July) 1933.

Weiss and Ellis studied the effects of sodium nitrite on the cardiovascular system of ten normal subjects and of forty-three patients with hypertension or nephritis. They found no correlation between the size of the dose and the extent of the symptoms, or between the latter and the drop in blood pressure. The pulse rate was increased in both groups, the average increase being eight beats per minute. Within thirty minutes, however, the heart rate had returned to its previous figure. The fall in blood pressure was manifest in from five to fifteen minutes after ingestion. In normal persons an average decrease of 12 mm. systolic and 10 mm. diastolic was observed. This persisted for about thirty minutes. In the patients the average fall in blood pressure was 35 mm. systolic and 20 mm. diastolic. The percentage decrease was of the same order of magnitude in both groups. In the patients, however, the blood pressure did not return to its previous figure for about two hours. Sodium nitrite appears to lower the blood pressure as a result of direct action on the smooth muscle of the wall of the vessel, causing peripheral arterial dilatation. The vasomotor center is either unaffected or slightly stimulated. Blood pressure cannot be maintained at a relatively low level by the routine use of sodium nitrite.

DAVIDSON, Newark, N. J.

CHANGES IN THE CENTRAL NERVOUS SYSTEM IN PROGRESSIVE MUSCULAR DYSTROPHY. JOSE MARIA JULIAN GIL, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **35**:116, 1933.

Histologic examination of the central nervous system in a case of progressive muscular dystrophy of thirty-four years' duration disclosed that the anterior horn cells were relatively intact except for a few cells in the dorsomedial group. The most intense changes were in the cells of the commissure and the adjacent cells and in the cells of the basal parts of the posterior horn. Special attention was given to a study of the hypothalamic region. The nucleus mamillo-infundibularis and the nucleus ansae peduncularis were intact, as were the nucleus paraventricularis, the nucleus supra-opticus and the small tuber cells. The significant changes in the cells of the commissure and the adjacent cells and the cells of the basal parts of the posterior horn varied from shrinkage to total destruction. The glial reaction was slight. The spinal cord also showed rich deposits of amyloid bodies extending from the thoracic to the sacral portion of the cord, meningofibrosis, edema and small hemorrhages. There were also some indefinite changes in the fibrillae, consisting especially of a netlike arrangement and clumping. Gil believes that the anatomic basis for the disease included only the changes in the cells of the commissure and in the basal posterior horn cells.

KESCHNER, New York.

NARCOLEPSY. S. BERNARD WORTIS and FOSTER KENNEDY. Am. J. Psychiat. **12**:939 (March) 1933.

Reviewing the hypotheses advanced in the literature to account for the development of narcoleptic attacks, Wortis and Kennedy conclude that it seems logical to consider this disorder as a syndrome denoting an underlying neurophysiologic derangement of an organic or physicochemical nature in or near the floor of the fourth ventricle and periaqueductal regions. The appearance of one or more of the following symptoms is characteristic of the disorder: (1) sleep or trancelike states which come on suddenly and irresistibly, and are often precipitated by acute

emotional states; (2) cataleptic spells in which the patient, though fully conscious, is helplessly immobile and semirigid, and (3) cataleptic attacks in which the patient falls to the ground with complete loss of skeletal muscular control, though he is quite relaxed, and fully conscious. During the latter state a positive Babinski sign is found, while the deep muscle tendon reflexes are not elicitable. Wortis and Kennedy report on the treatment of six patients suffering from narcolepsy. Five had cataleptic seizures. Four of the five were helped by the use of ephedrine sulphate in ¾ grain (0.04 Gm.) doses, three times daily. Narcoleptic attacks were relieved by this method in only two of the six patients. In most of the cases thyroid and caffeine sodium benzoate were ineffective.

DAVIDSON, Newark, N. J.

STUDIES ON CEREBROSPINAL FLUID: I. CHEMICAL AND SPECTROGRAPHIC DETECTION OF LEAD. I. M. RABINOWITCH, A. DINGWALL and F. H. MACKAY, J. Biol. Chem. **103**:707 (Dec.) 1933.

The authors have compared one chemical method with one spectrographic method for the detection of lead in cerebrospinal fluid. They give exact details of both procedures. The Behrens-Kley triple nitrite reaction as applied to biologic materials by Fairhall was found to be satisfactory for the detection of minute quantities of lead only if extreme precautions were taken to avoid contamination. They discuss the purification of the reagents and the necessity for using pyrex glassware throughout the test. Precautions are enumerated for avoiding contamination during evaporation and ashing of the specimens. There are so many possible sources of contamination that in spite of the many difficulties in isolating minute quantities of lead from cerebrospinal fluid, lead may be found by this test when it is not present in the original material. The spectrographic analysis was used as a control. This method is more sensitive than the chemical method, but many of the possible sources of contamination are eliminated. They conclude, therefore, that if lead is not found by the spectrographic method but is found by the chemical method, the lead so found is present as the result of contamination.

DAILEY, Boston.

THE TREATMENT OF EPILEPSY WITH BORATES. T. BOVET, Schweiz. Arch. f. Neurol. u. Psychiat. **31**:25, 1933.

Of seventy-two institutionalized persons with epilepsy treated with borate preparations for periods of from six to twelve months or longer, eleven showed marked improvement and thirteen lesser degrees of improvement. The borates were employed as adjuvants to the common drugs used in the treatment of epilepsy, which could be omitted entirely in only one case. Sodium borotartrate, which was administered in daily doses of from 6 to 10 Gm., was found not only to be less toxic, but also more effective therapeutically than either sodium tetraborate (borax) or boric acid. The treatment with borates gave rise to cutaneous eruptions in ten cases, polyuria in three and mental confusion with insomnia in five others. Persons of the asthenic or schizoid type seemed to be particularly good subjects for this form of treatment. Improvement, when it occurred, was usually noted within a week or two, although occasionally it became evident as late as two months after the beginning of treatment. A review of the literature, as well as his own experience, led the author to conclude that the beneficial effect of borates is probably attributable to an increased breaking down of fats and proteins and possibly to the production of acidosis, as well as to a dehydration.

DANIELS, Denver.

EFFECT OF MENSTRUATION ON THE INCIDENCE OF DEMENTIA PARALYTICA. RUDOLPH HECHT, Arch. Dermat. & Syph. **27**:568 (April) 1933.

Demonstrating by a statistical study that the incidence of early syphilis in females is about equal to that in males in the same social group, Hecht shows that dementia

paralytica is three times as common in men as in women. The biochemical changes associated with menstruation appear to be responsible for this relative immunity, and the disproportionately large number of women with dementia paralytica over the age of 50 suggests that the menopause removes this protective influence. During the premenstruum the capillaries show increased permeability, acidity is increased, cholesterol decreased, carbon dioxide concentration lessened, enzyme activity increased, and intermediary oxidation reduced. The process has a lytic effect on the storehouses of the spirochetes, giving the female ideal antisyphilitic treatment by mobilization and destruction of the organisms. At each menstrual period, therefore, the female undergoes an upheaval and adjustment, comparable in many respects to that following protein therapy; a woman with syphilis thus experiences each month a nonspecific shock reaction which may act to prevent the development of neurosyphilis in later life. The study is purely statistical, no experimental or clinical work in support of the hypothesis being cited.

DAVIDSON, Newark, N. J.

THE QUILL MECHANISM OF THE PORCUPINE: A STUDY OF THE AUTONOMIC NERVOUS SYSTEM. CURT P. RICHTER and ORTHELLO R. LANGWORTHY, J. f. Psychol. u. Neurol. **45**:143, 1933.

Erection of the quills of the porcupine depends on the contraction of the well developed smooth musculature in the vicinity of the quill follicles; the superficial striated muscle, the panniculus carnosus, does not participate in the movement of the quills. After removal of the preganglionic sympathetic chain on one side, there was no elevation of the quills on that side. The movement of the quills is under the control of the sympathetic portion of the autonomic nervous system. Stimulation of the cerebral motor cortex or other portions of the forebrain produced no elevation of the quills. Application of the electrode to an optic colliculus was followed, after a considerable latent period, by a slow raising of the quills, which was most marked on the opposite side of the body. Stimulation of the tectospinal tract produced an erection of the quills, predominatingly on the side stimulated. The erection of the quills was associated with quick movements of the tail. The authors conclude that there exists in the porcupine a unique mechanism of defense, partly under somatic control and partly under autonomic control, correlated in the optic colliculus under the guidance of visual stimuli.

KESCHNER, New York.

THE HOMELESS BOYS' RETREAT. JOHN LEVY, Ment. Hyg. **17**:369 (July) 1933.

On the basis of many psychiatric interviews with homeless boys passing through New York, Levy discusses the causes and results of the problem which they present. A quarter of a million adolescent boys are drifting around the country, looking for work. They travel alone, their desperate need for serving themselves first breeding a bitter selfishness. The journeys began as a healthy adolescent revolt against unfortunate home situations. The zest is gone by now, the lightheartedness and humor which are supposed to characterize the young wanderers have been replaced by suspicion, sullenness and egocentricity. Levy suggests that the personality development might have been served better by remaining at home, cheerless and hopeless as the prospect is; home, at least, would have provided congenial human contacts—the neighborhood "gang" if nothing else. Treated leniently by authorities, devoid of any philosophic background, possessed of no class consciousness, these boys have not become socialists; each still hopes to achieve salvation through his own efforts. The personalities of the boys will probably be seriously distorted and embittered, however, and prosperity alone will never give them back their senses of humor and their well integrated personalities.

DAVIDSON, Newark, N. J.

THE INFLUENCE OF THE DEVELOPING FORE LIMB ON NERVES ARISING FROM HETEROTOPIC SPINAL CORD TRANSPLANTS IN AMBLYSTOMA. W. M. ROGERS, Anat. Rec. **58**:71, 1933.

The brachial region of the spinal cord was implanted into heterotopic positions adjacent to the limb anlage. This graft was placed in four different orientations with respect to the limb disk, viz., ventral, dorsal, posterior and anterior, with the following results: 1. In each of these locations, spinal nerves and ganglia developed from the grafted cord, but a typical pattern was maintained only when the adjacent somites were included in the implant. 2. Although neurons differentiated from every isolated heterotopic cord, the degree of development was influenced by their orientation with respect to the limb-forming territory. When the implant lay ventral to the limb bud, nerves arising from the extraneous cord did not grow into the developing limb. 3. The size of the spinal nerves and their dorsal roots and sensory ganglia was dependent on the size of the territory which they supplied. Their size was about normal if they innervated approximately the same area as did the nerves on the side not operated on. They were hypoplastic if they supplied a smaller region and hyperplastic if the field innervated was unusually large.

COBB, Boston.

INDIVIDUAL MENTAL HYGIENE. WILLIAM B. TERHUNE, Ment. Hyg. **17**:10 (Jan.) 1933.

Defining individual mental hygiene as the personal application of the principles of mental health so directed as to improve efficiency, decrease mental sickness and widen the opportunities for happiness, Terhune gives several suggestions for individual behavior. These are: 1. Accept adaptation as necessary and possible. Realize that with proper direction of energies adjustment toward almost any situation can be made. 2. See situations as they are, not as they should be. 3. Budget daily activities so as to provide adequate time for rest, exercise and play. 4. Utilize the present wealth of spare time for the performance of serious and satisfaction-giving work. 5. Develop a good-natured, tolerant contempt for emotions; recognize them; do not act on them unless they are useful sentiments. Restrain or ignore self-pitying feelings, jealousy, suspicion, envy and revenge; utilize the worthy sentiments: loyalty, courage and kindness. 6. Use intelligence; develop it by serious intellectual pursuits so that it may be ready when the need arises. This program can be the individual's contribution to the sick world. Utilized on a large scale, it would materially advance general human happiness.

DAVIDSON, Newark, N. J.

THE FACTOR OF HYPOGLYCAEMIA IN THE AETIOLOGY OF IDIOPATHIC EPILEPSY. R. L. HAVILAND MINCHIN, J. Ment. Sc. **79**:659, 1933.

Examination of the blood sugar during fasting in eighty patients showed that the average value was 84.9 mg. per hundred cubic centimeters. This is believed by the author to be lower than the average. He postulates that hypoglycemia may be related to the tendency to convulsions, following the old observation that experimentally induced hypoglycemia usually causes convulsions. A dextrose tolerance test was carried out on sixty-six patients; 75 per cent had subnormal peaks. That is, in these patients the peak was below 150 mg. The author believes that the increasing secretion of the pancreas is responsible for the lowered blood sugar and, secondarily, the convulsions in persons with epilepsy. When drugs such as phenobarbital were administered the blood sugar rose. In the postconvulsive phase of epilepsy the immunity from fits is associated with increased blood sugar. Injections of atropine and physostigmine had no appreciable effect on the frequency and severity of convulsions. The author believes that the process of recovery in epilepsy is associated with decrease in secretion by the islets of Langerhans.

KASANIN, Howard, R. I.

THE ACTIVITY OF THE PITUITARY GLAND IN EXCITATION OF THE HYPOTHALAMUS. J. P. KARPLUS and O. PECZENIK, Arch. f. d. ges. Physiol. **232**: 402, 1933.

Former experiments of Karplus and Peczenik had shown that after stimulation of the hypothalamus in cats the cerebrospinal fluid acts more strongly than before the stimulation on the uterus in guinea-pigs and on the melanophores in frogs. This was interpreted as being due to an increased content of the pituitary products in the cerebrospinal fluid. In the present investigation Zondek and Krohn's "intermedin reaction" of the cerebrospinal fluid (i. e., its effect on the red pigment cells of Phoxinus laevis) was studied before and after stimulation of the hypothalamus. According to Zondek and Krohn, this reaction is caused by a product of the lobus intermedius of the pituitary gland. After stimulation of the hypothalamus in cats the cerebrospinal fluid shows a marked increase of the intermedin reaction. Furthermore, the effect of intravenous injections of the cerebrospinal fluid on the blood pressure was tested. Stimulation of the hypothalamus increases the pressor effect of the cerebrospinal fluid. The experiments corroborate the assumption that the hypothalamus regulates the secretory activity of the pituitary gland.

SPIEGEL, Philadelphia.

EXPERIMENTAL ALOPECIA. B. BARKER BEESON and WILLIAM J. PICKETT, Arch. Dermat. & Syph. **28**:53 (July) 1933.

Neurosurgeons will be interested in the production of areas of baldness by removal of the spinal ganglion of the second cervical nerve and its roots. This operation was first reported by Max Joseph in 1886. The authors operated on thirty cats under chloroform anesthesia. Mature animals were used. A medial incision was made from the occiput to the fifth cervical vertebra. The underlying tissues having been separated or incised, the ganglion was located deeply embedded in the muscles, 2 or 3 mm. from the median line, outside the spinal canal. This ganglion is well located for experimental purposes, emerging between the arches of the axis and atlas rather than through a special intervertebral foramen. From 2 to 5 mm. of each root was removed with the ganglion. Of the seventeen cats which survived, six showed alopecia areata. This developed within four days in one cat, within thirty days in another, and at intervening times in the remaining animals. The bald spots were located close to the occipital region, near the ears, and over the throat; they were bilateral and more or less symmetrical. The results point to a control of the growth of hair by the vegetative nervous system.

DAVIDSON, Newark, N. J.

ON THE NERVOUS CONTROL OF ABDOMINAL BLOOD VESSELS AND VISCERA. D. T. BARRY, Brit. M. J. **2**:373 (Aug. 26) 1933.

The problem dealt with in this paper concerns the rôle of parasympathetic and sympathetic systems in the regulation of muscular movements and vascular conditions in the abdominal viscera. The report is summarized by the author as follows: "The vagus nerves were stimulated peripherally below the origin of the cardio-inhibitor fibers. Motor effects on the intestine were obtained which were abolished by atropine and not affected by sympathetic paralysants. They are occasioned by parasympathetic fibers which really exist as myelinated units separate from the sympathetic. Inhibitory vagal fibers to stomach and intestine may be sympathetic in type. Vascular fibers exist in the vagus which on excitation yield hypertension and hypotension. These are unaffected by atropine, and are paralysed by ergot and yohimbine. They seem to be sympathetic elements. It is not possible to say if these occur in the vagus as pre- or post-ganglionic fibers. Stimulation of the vagus causes constriction of the kidney, but the reaction is well marked only in a certain proportion of animals. The nervous units responsible for this reaction behave like sympathetic elements."

FERGUSON, Niagara Falls, N. Y.

ORDER OF BIRTH IN MANIC-DEPRESSIVE REACTIONS. HAROLD H. BERMAN, Psychiatric Quart. **7**:430 (July) 1933.

Investigating the ordinal position in the family, Berman studied the records of one hundred patients with manic-depressive insanity. Forty-eight of these were first born; in every classification of family size there were more first-born persons among the group of patients than younger children. In families of two children, 70 per cent of the patients were first born; in families of three, 58 per cent, and in families of four, 57 per cent. In attempting to explain this predominance Berman mentions but does not discuss the possibility of greater exposure to head trauma in passing through a primiparous birth canal. He is inclined to explain the phenomenon on a psychic basis, as the jealousy of the older child toward the suddenly appearing baby, stealing his (the older's) position of importance. He suggests that many of the cases of "nervous breakdown," "nervousness," "weakness" and "sickliness" among children are really early or abortive manic-depressive attacks. If an effort is made to rebuild the destroyed feeling of superiority and importance in such children it may be possible to lessen the intensity and frequency of subsequent psychotic attacks.

DAVIDSON, Newark, N. J.

TUBERCULOUS CHARACTER AND TUBERCULOUS PSYCHOSES. H. STEFAN, Arch. f. Psychiat. **100**:352, 1933.

In a discussion of the literature on this subject and in relation to cases studied by the author, the conclusion is reached that one is justified in speaking of certain types of changes in the personality of patients suffering from tuberculosis. These are probably a result of the combined effect of the toxic agents associated with the disease as well as the psychic response of a person suffering from such a chronic ailment. The reaction is characterized by increased vegetative and other somatic irritability, a lability of mood which oscillates between euphoria and depression and a reduction of the general physical and mental tension and resistance of the person. In addition to this, however, definite types of psychoses are caused by the disease. The author reports a typical case of a woman, aged 26, suffering from acute disseminated hematogenous tuberculosis during the process of which there occurred a mental disease characterized by hallucinatory states, deterioration, disturbances of association and fantastic delusions. The psychosis was probably due to the direct effects of the toxic agent.

MALAMUD, Iowa City.

FIRST AID TO THE NEWLY ARRIVED PATIENT IN THE PUBLIC HOSPITAL FOR MENTAL DISEASES. RICHARD DEWEY, Am. J. Psychiat. **13**:299 (Sept.) 1933.

The importance of making a favorable impression on the newly arrived patient in a hospital for mental diseases is stressed by Dewey. He recommends that the reception of the new patient be made similar to the arrival of a guest at a hotel, by introducing an element of good will and personal interest. Not only is this the humane procedure, but it makes the patient more accessible to diagnostic and therapeutic approach. Dewey points out that even apparently demented patients can understand and appreciate a kindly attitude. The preliminary procedures, such as examination, removal of the patient's personal effects and administration of baths and medicines, should be courteously explained. A little refreshment, solid or liquid, may be pleasantly offered to the patient; the receiving officer should radiate cheer and good humor. The physician should see the new patient as promptly as possible, and the nurse should not say that the "doctor is too busy today; he will see you tomorrow." The entire course of the patient's psychosis may be determined by the circumstances of his reception.

DAVIDSON, Newark, N. J.

THE PATHOGENESIS OF CERTAIN ANISOCORIAS AFTER CRANIAL TRAUMATISM. G. WEILL and J. NORDMANN, Rev. d'oto-neuro-opht. **11**:516 (July-Aug.) 1933.

Aside from lesions of the third nerves from cranial traumatism (mydriasis and diminished pupillary reflectivity), other pupillar inequalities have been observed. The reflexes are normal, and in general it is the narrow pupil that is abnormal. All who have studied this question have at first attributed them to a sympathetic disturbance, but Landolt and Lafon renounced this assumption. Weill and Nordmann have sought for a concomitant symptom that would determine the question. In one case they found unilateral sweating of the face on the side of the narrow pupil, but Lafon had reported a case in which the sweating was on the healthy side. In another case, in which a tumor of the frontal lobe had been removed, a narrowing of the palpebral slit, myosis and enophthalmos appeared on the same side; the pupillar reactions remained normal. This oculosympathetic syndrome persisted for several years. This case proves that these anisocorias may be accompanied by a well marked sympathetic syndrome. DENNIS, San Diego, Calif.

INFLUENCE OF THE PARATHYROID ON THE METABOLISM OF CREATINE AND PHOSPHORIC ACID. C. G. IMRIE and C. N. JENKINSON, Physiol. **79**:218 (Sept. 4) 1933.

Experiments described in this paper show that in thyroparathyroidectomized cats the concentration of creatine phosphate in the muscles is lower than in normal cats; also that the rate of resynthesis of creatine phosphate following stimulation of the muscles is much slower in the former than in the latter animals. It has also been shown clearly that, following the administration of parathormone to thyroparathyroidectomized cats, the resynthesis of creatine phosphate after its concentration in the muscle has been lowered by stimulation takes place at a rate similar to that observed in normal animals. This effect of the parathormone is manifest within at least five hours after its intravenous administration. When creatine is administered along with parathormone in feeding experiments lasting several days or in acute experiments there appears to be a definite effect on the initial content of the creatine phosphate in the muscles and on the rate of resynthesis after stimulation. ALPERS, Philadelphia.

PARADOXICAL TONUS IN CEREBELLAR LESIONS. A. AUSTREGESILO, Rev. neurol. **1**:637 (May) 1933.

In this report the author discusses the question of alternating hypertonia and hypotonia which is so often seen in cerebellar lesions. He first gives his views on the physiology of the cerebellum, which agree on the whole with those of Luciani, Mills and Weisenburg, namely, that its principal function is that of synergy and that the earliest and most important signs of cerebellar dysfunction are incoordination, ataxia and dysdiadokokinesia. The study included classic cerebellar syndromes and infantile encephalopathies. He found that alterations of tonus are frequent in these conditions; that repeated passive movements often bring out a latent hypertonicity; that the upright position frequently brings about a change from hypotonia to hypertonia, and finally, that stimulation of the labyrinth will often produce this same change. He concludes that these changes may be explained by the close relationship of the cerebellum with the tonic centers, by way of its superior peduncle, and with the bulbar nuclei, particularly with Deiters' nucleus, by way of its inferior peduncle. SCHNEIDER, Washington. D. C.

A REVIEW OF ONE HUNDRED AND FIFTY CASES OPERATED ON UNDER SPINAL ANESTHESIA. B. M. SUNDARAVADANAN, M. S. Suggestions **2**:37 (Feb.) 1933.

To prevent postoperative shock, afford perfect muscular relaxation, reduce straining and avoid the preoperative and postoperative periods of starvation, the

author recommends the use of spinal anesthesia. The medication used in the series reported was 7.5 per cent procaine hydrochloride in a solution of 5 per cent dextrose. About 2 cc. of this solution is injected into the subarachnoid space after an equal amount of fluid has been withdrawn. The upper level of analgesia should always be determined by pinpoint testing. In only four of the one hundred and fifty cases did headache persist for more than a day, and in these instances acetylsalicylic acid afforded relief. Backache was not severe and catheterization was necessary in only seven or eight patients. No serious drop in blood pressure was noted. Spinal anesthesia should not be used on patients who are highly nervous, but otherwise there are substantially no contraindications.

DAVIDSON, Newark, N. J.

FURTHER STUDIES OF THE FLEXOR RIGIDITY OF THE HINDLEGS IN THE MALE SPINAL CAT. J. G. DUSSER DE BARENNE and Y. D. KOSKOFF, Arch. f. d. ges. Physiol. **232**:56, 1933.

The authors had observed in decerebrated cats, particularly in male animals, that a "secondary" decapitation or transverse section of the spinal cord in the first lumbar segment is followed by the development of a flexor rigidity of the hindlegs and marked priapism if the hind part of the body is placed symmetrically on the table. Further studies showed that these phenomena develop even if transverse section of the cord is performed without preceding decerebration. This rigidity is a reflex phenomenon; it disappears after severance of the posterior roots in the lumbosacral segments, or if the hind part of the body lies on the side or on the back or if it is held in the air. The impulses which elicit this reflex take their origin from the ventral surface of the abdomen and of the hindlegs. These parts must touch the table and the hindlegs must lie sprawling in order to produce this reflex. Impulses from the anterior part of the body or from the lumbosacral parts of the spine can change this rigidity.

SPIEGEL, Philadelphia.

AN UNUSUAL DERMATOSIS FOLLOWING SECTION OF THE FIFTH CRANIAL NERVE. ADOLPH B. LOVEMAN, Arch. Dermat. & Syph. **28**:369 (Sept.) 1933.

Postoperative complications following radical operations for tic douloureux are comparatively rare. Dermatoses are exceedingly rare. Loveman reports a unique case of postoperative ulceration closely resembling carcinoma. The patient had been suffering from neuralgia of the trigeminal nerve for eight years, and in 1928 a radical resection of the sensory root of the left gasserian ganglion was performed. There were no immediate postoperative complications, but six weeks later a trophic ulcer developed in the left nostril. Nine months later a swelling of the left lower eyelid appeared, accompanied by a discharging lesion of the left side of the upper part of the forehead. When the patient was again seen, three years after the previous examination, she presented an extensive ulceration over the left side of the nose, forehead and scalp, with an adjacent area of baldness. Histologically, the lesions resembled carcinoma, but the condition was finally diagnosed as benign epithelial hyperplasia. The ulcers healed under roentgen treatment.

DAVIDSON, Newark, N. J.

THE INFLUENCE OF DIFFERENT HORMONES (ACETYLCHOLINE, INSULIN, THYROXIN, THYMUS EXTRACTS) ON THE EFFICIENCY OF FROG'S MUSCLES AND ON THE DEVELOPMENT OF CONTRACTURE. O. WEBER, Arch. f. d. ges. Physiol. **232**:727, 1933.

Acetylcholine, in doses of from 0.004 to 0.4 mg. per cubic centimeter, delays fatigue; concentrations above 1 mg. per cubic centimeter are noxious. Insulin, in doses of from 0.005 to 0.02 unit per cubic centimeter, improves the efficiency; concentrations above 0.4 unit per cubic centimeter injure the muscles. The development of acetylcholine contracture is influenced in a similar way; yet very

weak concentrations (0.002 unit per cubic centimeter) lower the contracture. Thyroxin, in dosage of 10 mg. per cubic centimeter, lowers the excitability as well as the contractibility. The influence on acetylcholine contracture was different in different muscles and showed also seasonal differences. Watery thymus extracts increase the acetylcholine reactions in the rectus abdominis and flexor carpi radialis, and lower these reactions in the sartorius and extensor metacarpi.

SPIEGEL, Philadelphia.

OPTIC NEURITIS ORIGINATING FROM SINUSITIS. Q. DI MARZIO and G. FERRERI, Ann. d'ocul. **170**:692 (Aug.) 1933.

Di Marzio and Ferreri studied the relation of optic neuritis, both edematous and retrobulbar, to disease of the nasal accessory sinuses, either confirmed or latent sinusitis. They studied and operated on thirty patients with various lesions of the optic nerve, accompanied by a considerable decrease of visual acuity. Opening of the ethmoid or sphenoid sinuses resulted in improvement of most patients, but the highest percentage of improvement was obtained when there was no evidence of sinusitis clinically, roentgenographically or at operation; next in importance is the percentage of improvement in forms of confirmed or latent sinusitis. Improvement or cure was noted as early as twenty-four hours after intervention. In other cases improvement occurred after several months or years. Patients showing improvement passed through several stages, from absolute central scotoma to relative scotoma and then to disappearance of the scotoma. The report is presented with numerous roentgenograms and charts of the visual fields.

BERENS, New York.

PSYCHOANALYSIS AND THE PRACTICING PHYSICIAN. DORIAN FEIGENBAUM, Zentralbl. f. Psychotherap. u. Grenzb. **6**:27, 1933.

This lecture was delivered before the German Medical Society of New York City. Its purpose was to give the practitioner of medicine, in brief form, an idea of what psychoanalysis is and of what practical use a knowledge of it may be to him. The scientific nature of the psychoanalytic method, which is being objectively guided and repeatedly checked, is briefly discussed. The rôle that psychoanalysis plays in medical psychotherapy is strikingly contrasted to that of suggestion in medical practice. Several clinical situations met with by the general practitioner are used to illustrate how a physician oriented in the basic principles of psychoanalysis may be in a position to sense the deeper significance of common psychic symptoms, to avoid dalliance with futile procedures and to be of real assistance to patients, either directly in helping them handle their own neurotic symptoms in certain cases or in directing them to early and proper treatment of complicated conditions.

MAEDER, Philadelphia.

FIXATION AND VOLUNTARY NYSTAGMUS. ALFRED F. LUHR and JOHN L. ECKEL, Arch. Ophth. **9**:625 (April) 1933.

Fixation nystagmus and voluntary nystagmus are both rather uncommon. In the first, nystagmus develops after intent fixation on some object at rest; in the second, the nystagmus occurs by will power alone, i. e., by concentration by the patient on the idea and the desire to make the eyes oscillate. Luhr and Eckel present two cases: the first of fixation and the second of voluntary nystagmus. Both are recorded as an ocular type of nystagmus. It is likely, however, that the mechanism of the formation of these types of nystagmus is rather different from that in ordinary ocular nystagmus. These authors believe, however, that probably the same underlying principle is present in the production of both types; that they are both functional in origin, and that they may be explained as the result of fatigue of the muscles resulting from the primary fixation of gaze plus frequent repetition of the process, and with the resulting imbalance between the agonist and antagonist muscles and oscillations.

SPAETH, Philadelphia.

INCIPIENT PAPILLEDEMA. M. DUHAMEL, Ann. d'ocul. **170**:711 (Aug.) 1933.

Duhamel presents a series of preparations of optic nerves affected with incipient papilledema which were fixed as soon as possible after death. From their study he derives the following conclusions: The edema begins in the intra-ocular portion of the optic nerve; it has a tendency to spread along the nerve toward the chiasm; it is absent where the nerve passes through the lamina cribrosa, but behind the lamina cribrosa it continues along the central vessels; after the exit from the central arteries the edema decreases in the interfascicular spaces and near the pial sheath; it is no longer present when the nerve passes through the bony canal. The subvaginal space is dilated along the entire optic nerve. When stasis persists, drainage along the central vessels becomes insufficient and the edema spreads above the vessels to the chiasm. The edema is caused by insufficiency of the ophthalmic vein, due partly to hypertension in the central artery and partly to circulatory disturbance resulting from the hypertension of the cerebrospinal fluid in the subvaginal space, which the vein crosses.

BERENS, New York.

A NEW TEST FOR VISUAL ACUITY. F. H. VERHOEFF, Arch. Ophth. **10**:226 (Aug.) 1933.

Vision is such a complicated phenomenon and is dependent on so many variables that no single test can be devised by which it may be measured accurately for all purposes. There is no doubt that, for practical purposes, the most important factor in estimating visual acuity is the resolving power of the eye. It is best measured by determining the minimum separable. While the Snellen test measures this fairly well, its chief disadvantage is that different letters, as utilized, are not all affected alike by astigmatism and other aberrations of the optic system and hence have different degrees of legibility. Various attempts have been made to improve on the Snellen test. but not with great satisfaction. Verhoeff has utilized a series of double and triple circles, believing that, regardless of the type of aberration present, an equal distortion will occur in each instance. The procedure should be of value in working out the finer details of this rather important functional test.

SPAETH, Philadelphia.

PURPURA HAEMORRHAGICA WITH CEREBROSPINAL HEMORRHAGE. A. J. GEIGER, J. A. M. A. **102**:1000 (March 31) 1934.

Geiger reports two cases of hemorrhagic purpura in one of which it seems probable that the bloody spinal fluid obtained by lumbar puncture during the first admission to the hospital arose from meningeal bleeding. The sudden development of hemiplegia associated with recurrence of active purpura some months later suggests that an extensive hemorrhage occurred within the cerebrum at this time. In the other case the period of observation was unfortunately too brief for satisfactory neurologic study, but the coma, convulsions and rapidly fatal course in the absence of localizing signs suggest either an intracerebral or a large subdural hemorrhage. Although cerebrospinal hemorrhage in purpura usually implies a fatal prognosis, recovery from even large hemorrhages has been reported. Recoveries seem commonest in the "meningitic group;" none have been noted in the group with hemiplegia.

EDITOR'S ABSTRACT.

THE CONTROL OF THE DERMAL MELANOPHORES IN ELASMOBRANCH FISHES. G. H. PARKER and H. PORTER, Biol. Bull. **66**:30 (Feb.) 1934.

The common dogfish, Mustelus canis, has a dark phase and a light phase owing to the expansion and the contraction of its dermal melanophores. The dark phase is induced by pituitary secretions carried from the pituitary gland to the melanophores by the blood and lymph, as described by Lundstrom and Bard. The light phase is induced through nerves acting on the melanophores and causing them to contract, and is not merely the result of the absence of pituitary secretions. The expanding hormone is water-soluble; the contracting one, if there is such, is

apparently not water-soluble. The dogfish is remarkable as the first form to be described in which the cutting of nerves induces a contraction of the melanophores and a consequent lightening of the skin.

COBB, Boston.

JUVENILE TYPES OF GENERAL PARALYSIS. R. M. STEWART, J. Ment. Sc. **79**:602, 1933.

Fourteen patients with juvenile dementia paralytica were studied by Stewart. In eight, mental defect appeared fairly early in life. In a second group, dementia started after a period of normal intellectual development. The age of onset is usually between the tenth and the sixteenth year, and the disease lasts longer than in the adult. The stigmas of congenital syphilis may be absent. In juvenile dementia paralytica neurologic signs are more common, such as complete immobility of the pupils and optic atrophy. The clinical picture is characterized by a simple progressive dementia, although occasionally grandiose and paranoid delusions appear. The pathologic process is characterized by the smallness of the hemispheres, status spongiosus of the cerebral cortex, atrophy of the cerebellar folia and binucleated Purkinje cells. The author is pessimistic about the results of treatment in juvenile dementia paralytica; none of his patients have improved.

KASANIN, Howard, R. I.

A CASE OF COMBINED SCLEROSIS WITHOUT ANAEMIA TREATED BY INTENSIVE IRON THERAPY. WILLIAM SARGANT, Brit. M. J. **1**:1100 (June 24) 1933.

A case is presented in which the symptoms of combined sclerosis of the cord without anemia were rather typical. The patient was treated with 150 grains (9.75 Gm.) of ferrous carbonate daily, with rather remarkable results. In commenting on this case, Wilfred Harris expressed the opinion that massive doses of iron, with or without the usual liver therapy, might be used in many cases of combined sclerosis. Symptoms of subacute combined degeneration occur at times with a normal blood picture. It is important to determine the presence of achlorhydria as a valuable point in differentiating the condition from tabes, disseminated sclerosis and toxic polyneuritis. Dr. Harris recommends treatment in all cases by the addition of iron and thinks that the degeneration of the spinal cord may in some way be dependent on deficient iron metabolism, which again may in part be associated with achlorhydria.

FERGUSON, Niagara Falls, N. Y.

COMPARISON OF THE CHEMICAL COMPOSITION OF AQUEOUS HUMOR, CEREBROSPINAL FLUID, LYMPH AND BLOOD FROM FROGS, HIGHER ANIMALS AND MAN: REDUCING SUBSTANCES, INORGANIC PHOSPHATE, URIC ACID, UREA. ARTHUR W. WALKER, J. Biol. Chem. **101**:269 (June) 1933.

The author found approximately the same concentration of reducing substances and inorganic phosphates in the lymph from the frog's web as in blood plasma. In cerebrospinal fluid of frogs he found that the concentration of reducing substances is about 30 per cent less than in plasma; that of inorganic phosphate, about 60 per cent less. The aqueous humor of frogs showed the same deficiency in reducing substances and inorganic phosphates as the cerebrospinal fluid. In higher animals the deficiency in phosphates in aqueous humor as compared to plasma was uniformly present; that of reducing substances was less marked. He concludes that the choroidal and ciliary epithelium exhibit selective qualities not possessed by the capillary endothelium or by the glomerular membrane.

DAILEY, Boston.

METABOLIC INVESTIGATIONS IN MYASTHENIA PSEUDOPARALYTICA. I. HELLICH and C. TESSENOW, Ztschr. f. d. ges. Neurol. u. Psychiat. **146**:219 (May) 1933.

Metabolic studies were made in a case of myasthenia gravis of ten years' standing. The level of lactic acid in the venous blood was elevated while the

patient was at rest, and that in the arterial blood was normal. In the evening, at the time of greatest fatigue, there was a slight increase in the level of lactic acid in the arterial blood, with a decrease in that in the venous blood. The blood calcium and magnesium were normal. The creatinine in the urine was normal. The observations indicate a disturbance in carbohydrate metabolism, the muscles having lost the power to build up glycogen. This does not explain, however, the great fatigability of the muscles in this disease, especially since it is known that there may be extensive disease of the liver and marked disturbance of carbohydrate metabolism without the occurrence of myasthenia.

ALPERS, Philadelphia.

ENCEPHALOGRAPHY IN ABNORMAL MENTAL STATES WITH DIABETES INSIPIDUS. PURCELL G. SCHUBE, J. Nerv. & Ment. Dis. **78**:453 (Nov.) 1933.

An encephalographic study of diabetes insipidus has never been previously reported, and the author undertakes a careful investigation of three cases of this rather rare condition. The actual pathology of this condition is unknown, although lesions of the floor of the third ventricle have been held responsible. In the three cases presented by the author the diagnosis was schizophrenia, epileptiform seizures and mental retardation, respectively, all in conjunction with diabetes insipidus. In two of the three cases removal of spinal fluid resulted in improvement; it made no change in the third so far as the diabetes insipidus was concerned. In the case of the patient with the epileptiform convulsions improvement occurred after the removal of spinal fluid. Roentgenograms showed no abnormality in the pituitary fossa, lateral ventricles and third ventricle.

HART, Greenwich, Conn.

THE TREATMENT OF PRIMARY DYSMENORRHEA, WITH SPECIAL REFERENCE TO ORGANOTHERAPY. EMIL NOVAK, Am. J. M. Sc. **185**:237 (Feb.) 1933.

Old views that dysmenorrhea is the result of an obstruction to the exit of menstrual blood and hypoplasia of the uterus are quickly dismissed. More difficult factors are encountered in the constitutional and psychogenic fields. The question of the hormonal regulation of uterine contractility has yielded good results in clinical application. Reynolds reported that the normal excitant of uterine contractility is the follicle hormone, while the corpus luteum, progestin, is an inhibitor. In treatment for the dysmenorrheic attack in the past, antispasmodic drugs (atropine sulphate) were indicated. For the future biologic inhibitors of uterine contractility, progestin and the luteinizing principle of the urine of pregnant women offer rational methods. For permanent relief, theelin is suggested for uterine hypoplasia. The psychogenic factor should always be borne in mind.

MICHAELS, Boston.

BASAL METABOLISM IN ASTHMA AND IN EPILEPSY. ANNE TOPPER and HANNAH MULIER, Am. J. Dis. Child. **46**:963 (Nov.) 1933.

The author studied the basal metabolic rate in twenty-five children with asthma and twenty-five children with so-called true epilepsy. Of the twenty-five with asthma, all showed a basal metabolic rate which was within normal limits; the majority had minus readings. Of the children with epilepsy, twenty-four had normal rates, and again the majority showed minus readings. They conclude that the metabolic rate tends to be lower in these children and that the lower rate should not be considered as an indication for the administration of thyroid. They believe that the lower rate may be evidence of a reduced amount of thyroxine in the tissues as the result of the excessive demand made on the thyroid gland during the convulsive or asthmatic attacks; it is therefore the result rather than the cause of the underlying true condition.

WAGGONER, Ann Arbor, Mich.

THE PROTEIN RELATIONSHIPS IN THE CEREBROSPINAL FLUID. H. STEFAN, Arch. f. Psychiat. **100**:289 (July) 1933.

In this paper Stefan reports the results of investigations of the protein in the cerebrospinal fluid in sixty-four cases by a method described by him previously (*Arch. f. Psychiat.* **99**:317, 1932). He reports the following findings: In normal persons the total protein was 21.5 mg., the globulin 3.6 and the albumin 19.8; the protein quotient (globulin divided by albumin) was 0.21. In untreated dementia paralytica the total protein was 83 mg., the globulin 50.6 and the albumin 32.7, with a quotient of 1.8; in cases of treated dementia paralytica the total protein was 96 mg., the globulin 34 and the albumin 35.5, with a quotient of 1. In schizophrenia the total protein was 42.8 mg., the globulin 8.6 and the albumin 34, with a quotient of 0.26. In cerebrospinal syphilis and tabes the total protein was 69 mg., the globulin 30.9 and the albumin 38.2, with a quotient of 0.8.

MALAMUD, Iowa City.

THE PROPRIOCEPTIVE CENTERS OF THE SPINOBULBOPONTOMESENCEPHALIC AXIS. J. NICOLESCO, Rev. neurol. **2**:361 (Sept.) 1933.

Nicolesco has been interested for a number of years in the large vesicular cells of the neuraxis, and believes that the cells of Clarke's column are homologous with those of Monakow's nucleus (which lies within the field of Burdach's nucleus) and particularly with those of the mesencephalic root of the fifth nerve. It is obvious that these underlie the function of proprioceptive activity and also that they are of ancient phylogenetic formation. The great development of the mesencephalic cells in birds is particularly remarkable. These vesicular cells constitute a system of neurons intercalated along the pathway of the tracts of proprioceptive sensibility. From the standpoint of comparative anatomy, it would seem that the mesencephalic cells may have to do with the sensibility of the extrinsic muscles of the eyeballs.

FREEMAN, Washington, D. C.

GUMMA OF THE HYPOPHYSIS AND HYPOTHALAMUS. E. B. FINK, Arch. Path. **15**:631 (May) 1933.

Gumma of the hypophysis is rare, less than thirty cases having been reported. In only five was there gummatous involvement of both the hypophysis and the interbrain. In the presence of signs of cerebral syphilis, the occurrence of hypopituitary symptoms, such as severe cachexia, amenorrhea or pituitary dystrophy, justifies a diagnosis of gumma of the hypophysis. Polyuria indicates involvement of the infundibulum or of the tuber cinereum. Tremor, weakness of the extremities, unstable gait, atrophy of the extremities and hypertonia may occur when the thalamus is destroyed by a gumma. Acromegaly cannot be caused by syphilitic involvement of the hypophysis, because syphilis always produces destructive effects in parenchymatous organs, whereas acromegaly is an expression of hyperfunction of the hypophysis.

WINKELMAN, Philadelphia.

THE FECAL FLORA IN CATATONIC DEMENTIA PRAECOX. BARBARA MCGINN, MARY RANEY and NICHOLAS KOPELOFF, Psychiatric Quart. **7**:260 (April) 1933.

The hypothesis that focal infection is the cause of mental disease will receive little support from the present work. The authors made repeated examinations of the feces of four patients with catatonic dementia praecox. All were on the standard hospital diet, and the study covered a period of four months. In each instance the flora was less putrefactive than might be expected, and the findings closely approximated the normal. No unusual microbes were found, nor was any significant variation noted in hydrogen ion concentration, total bacterial count or predominant type of organism. The incidence of Lactobacillus acidophilus was less than normal, but the flora was fermentative rather than putrefactive.

DAVIDSON, Newark, N. J.

SOME REMARKS ON THE TREATMENT OF GENERAL PARALYSIS BY DIATHERMY. NORMAN B. GRAHAM, J. Ment. Sc. **79**:89, 1933.

Graham has treated twenty-four patients with dementia paralytica by diathermy. Each patient was kept at a temperature between 104 and 106 F. for four hours. Two or three treatments were given after apparent remission had taken place. He emphasizes the need of extreme caution, as one patient died; however, she was a poor risk to begin with. It is difficult to control the temperature; in one case it shot up suddenly to 106.8 F. Treatments were given once in ten days; although there was initial loss of weight after the treatment, there was an increase toward the end of the ten day period which averaged 2 pounds (0.9 Kg.). In 52 per cent of the cases clinical remission took place, and for this reason Graham concludes that his results are superior to those obtained by treatment with malaria.

KASANIN, Howard, R. I.

THE PROBLEM OF DIFFUSE SCLEROSIS. W. BENOIT, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:517 (July) 1932.

Kufs believes that diffuse sclerosis and multiple sclerosis belong to one vasologic group. He believes that transitions occur between these two groups, which are really parts of one pathogenic process. Benoit reports a group of cases which do not bear out this contention. In two cases there was extensive demyelinization of the white matter, with sparing of the arcuate fibers. No formation of tumor was found and no inflammatory process established. In one case there were typical foci of multiple sclerosis in the spinal cord and areas of demyelinization typical of diffuse sclerosis in the brain. Benoit does not believe that they represent transition forms because the argentophil bodies of Steiner, said to be pathognomonic of multiple sclerosis, were present in the areas of multiple sclerosis but not in those of diffuse sclerosis.

ON VASO-DILATOR FIBERS IN THE SYMPATHETIC AND ON THE EFFECT OF CIRCULATING ADRENALINE IN AUGMENTING TRUE VASCULAR RESPONSE TO SYMPATHETIC STIMULATION. J. H. BURN, J. Physiol. **75**:144 (June 21) 1932.

In this article is presented evidence of the existence of vasodilator fibers in the lumbar sympathetic chain of the dog. The preparation which was used enabled the changes produced by stimulation of the sympathetic nervous system to be observed in the main vessels, from the abdominal aorta downward. It is also shown that the magnitude of the vascular response to stimulation of the sympathetic nervous system, whether constrictor or dilator, not only is increased by the presence of circulating epinephrine but is dependent on the amount of epinephrine in the circulating blood.

THE EFFECT OF FATIGUE ON END PLATE DELAY. W. G. WALTER, J. Physiol. **76**:116 (Sept.) 1932.

Measurements were made of the delay in the transmission of activity from nerve to muscle by leading off the electrical charges in both to an amplifier and a Matthews oscillograph. It was found that fatigue caused no increase in the delay when a sartorius-nerve preparation was used. Observation of the changes in the conduction rate of muscles resulting from fatigue indicates that the changes hitherto attributed to an intermediary substance were changes in the characteristics of the muscle. Walter suggests that there is no need to postulate either a slower conduction rate in the terminal nerve fibers or the existence of a separate substance in order to account for the delay, which is less than the duration of the nerve action potential.

CONTRIBUTION TO THE ETIOLOGY OF FACIAL HEMIATROPHY. M. CHASANOW, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:473 (July) 1932.

Chasanow says that facial hemiatrophy is to be regarded as a partial manifestation of scleroderma and often as the first sign of scleroderma. Clinically, in these cases there are often other signs of scleroderma. Vegetative changes are at the basis of the disorder and can be demonstrated in the cervical ganglia, especially in the superior cervical ganglion. This is shown by the Horner syndrome, atrophy of the tongue and other signs. Injury of the vegetative system at the base of the brain can also lead to sclerotic processes in the muscles, bones and other tissues. Congenital factors play an important rôle in the production of facial hemiatrophy.

VESTIBULAR EFFECT ON BODY MUSCULATURE. H. ALTENBURGER and H. G. WOLFF, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:657 (Feb.) 1932.

Altenburger and Wolff set out to determine whether stimulation of the vestibular nerve produced a change in body musculature demonstrable through motor chronaxia. They studied the chronaxia in antagonists on both sides of the body in twenty-five subjects. They found that in vestibular stimulation (hot, cold or rotation) the chronaxia of the extensor muscles is decreased, while that of the flexor muscles is increased or remains unchanged. The same holds true for abductors and adductors, except that the changes are slighter. The effect is probably produced through the anterior horn cells by means of the vestibulospinal path.

THE SUPERNORMAL PHASE IN MUSCULAR CONTRACTION. TAKEO KAMADO, J. Physiol. **76**:189 (Oct. 4) 1932.

Kamado found that if a regular series of single shocks was given to a gastrocnemius muscle through its nerve, its tension-time response increased until a stationary level was attained. Increasing the stimulation interval caused a fall, decreasing the interval caused a rise in the level—so far as this is not affected by the onset of fatigue or by the relatively refractory period. The so-called supernormal response, at least in the case of the tension-time of a contraction, can be regarded as the first step toward a change in the steady level due to a sudden change of the stimulation interval.

THE RESORPTION OF CIRCULATORY TOXINS (EPINEPHRINE, ACETYLCHOLINE, HISTAMINE) FROM THE CENTRAL NERVOUS SYSTEM. A. FREYTAG and E. SCHIEF, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:35 (Feb.) 1932.

The resorption of toxins such as epinephrine, histamine and acetylcholine into the blood stream in intracerebral and subdural injections occurs so quickly that there is no important time difference between a circulatory effect after intravenous injection and that after intracerebral or subdural injection.

ENDOCRINE INSUFFICIENCY AND THE BRAIN. M. SEREJSKI and R. TOPSTEIN, Ztschr. f. d. ges. Neurol. u. Psychiat. **141**:65 (Aug.) 1932.

Serejski and Topstein performed thyroidectomies on dogs and killed them two to four and one-half months after operation. Chemical studies of the brain revealed an increase in the water content and a decrease in cholesterol, lipoids and unsaturated phosphatides.

ALPERS, Philadelphia.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, April 19, 1934

PERCIVAL BAILEY, M.D., *President, in the Chair*

TRAUMATIC ENCEPHALOPATHY IN PROFESSIONAL PUGILISTS. DR. HARRY L. PARKER, Rochester, Minn. (by invitation).

The discussion centers on the after-career of three pugilists. In each, during the period of active fighting, certain neurologic syndromes appeared which progressed up to a certain point and then remained about stationary. These were characterized largely by spasticity, tremor and ataxia. In one patient the condition was at its worst for a few days following a severe beating in the ring. In the other two patients the progression of events was slow and insidious for a number of months or years after they left the ring. Syphilis and encephalitis were excluded as far as possible. Apparently there are three possible types of injury in professional pugilism. The first occurs during the fight and leads to death or disablement directly as the result of a particular injury received during one bout. In the second type neurologic symptoms develop within a few days or weeks after the fight, also leading to death or disablement—for example, subdural hematoma. The third type is the one considered in the paper, characterized by the insidious, progressive development of neurologic symptoms during the height of the pugilist's career.

DISCUSSION

DR. FRANCIS J. GERTY: I have examined three prize-fighters, two at the Psychopathic Hospital and one in private practice. One of these men was not a "top-notcher." He had been a sparring partner and was a brother of a leading contender for the light-weight championship. He had taken up sparring because members of his family were in the profession, but he was never very good. He had cauliflower ears and was pretty well scarred. He had schizophrenia and was sent to the Elgin State Hospital. The second patient was not a champion but had been beaten by a light-weight champion. His excuse for the loss of this fight was that he was blind in one eye from an injury. He had a detached retina. The reason for which I saw him had no connection with his profession. He had dementia paralytica of the tabetic form. The third patient was champion of the world about twenty years ago. He was regarded as being courageous and able to "take more punishment than any man who had ever fought." In an autobiography he published in 1909 he included a newspaper article by Jack London, who reported the fight in which he won the championship. London referred to him as "the abysmal brute." This man was in trouble in 1927 for having published some moving pictures of one of his fights without first obtaining title to them. The municipal judge thought that there was something wrong with him mentally because he had a peculiar laugh and acted queerly. He was sent to the Psychopathic Hospital for observation. No psychosis or dementia was found but the man laughed peculiarly and delighted in shadow boxing and dancing around the wards. His usual gait had some fancy movements in it, although no pathologic condition could be discovered. The pupils were absolutely fixed; they did not react to light or in accommodation. The blood and spinal fluid were normal; he did not use alcohol, and there had been no venereal infection so far as could be determined.

DR. PERCIVAL BAILEY: I understood Dr. Parker to intimate that these syndromes are a little different from those following a single injury, such as being

run over by an automobile. I have seen many patients with peculiar syndromes following one injury, and I wonder whether he meant to emphasize the repetition of the injury as the essential factor.

DR. G. B. HASSIN: About a year ago the newspapers reported the case of a youth, aged 20, who died following a prize-fight of two rounds. The boy rode on an elevated train and walked about five blocks to his home, where he complained of headache, vomited repeatedly and died two hours after the fight. Necropsy did not reveal any injury to the brain or blood vessels or any external injuries, but 2 ounces (58 cc.) of blood was found subdurally over the right parietal region. A similar case occurred in New York. Probably the pathologic changes in the parenchyma of the brain are not hemorrhages but other changes in the form of concussion with subsequent formation of multiple scars. These do not extend and are most likely responsible for the stationary symptoms that Dr. Parker so well described.

DR. HARRY L. PARKER: I think that there is nothing so controversial as trying to show an association between injury and the conditions that follow. I tried to make plain that so far as possible in the cases presented every possibility was excluded other than that the repeated injury to the head during the patient's active pugilistic career was responsible for the condition. I grant that syphilis is relatively common among pugilists. There is no reason why they should not have it, and no reason why it should not produce the clinical syndromes I have described. There is also the question of coincidence, and this must always be excluded if possible. I think, however, that in some pugilists, as the result of repeated injury to the head, this syndrome develops, which progresses as long as they continue to fight and stops when their punching career is over.

I may have misled Dr. Bailey in saying that the conditions in these cases are different from those that follow a single injury. They are different only in that the injuries are multiple. The results may be identical. They differ in the fact that the patient, instead of receiving one injury, receives many, and the history is therefore different. What the pathologic changes were that occurred in these cases I do not know. Martland described several things, and theorized about them. Personally, I think that to theorize is a mistake until at least a little is known about the underlying pathologic processes.

DR. PERCIVAL BAILEY: As I said, I have seen parkinsonian syndromes following a single injury to the head and have always had difficulty in trying to convince myself that the condition was due entirely to the injury. I was rather surprised that Dr. Parker's second patient had not sued the steel company, for he would have had as good an excuse as many others who bring suit against their employers.

THE PHYSIOLOGY AND PATHOLOGIC PHYSIOLOGY OF THE PITUITARY GLAND AND ADJACENT STRUCTURES. DR. ARNO B. LUCKHARDT (by invitation).

(After reviewing the embryology and physiologic anatomy of the hypophysis, the effects of hypophysectomy, tuberectomy and irritative lesions in the corpora mamillaria and tuber cinereum, the effects of extracts of the anterior lobe [the thyrotropic, gonadotropic, growth-promoting and lactogenic substances and the fat metabolism enzyme] and of the posterior lobe [pitressin, pitocin and the melanophore substances], Luckhardt discussed the following syndromes and conditions and their relation to lesions in and about the hypophysis: acromegaly and gigantism, Fröhlich's syndrome [dystrophia adiposogenitalis], hypophyseal cachexia [Simmonds' disease], diabetes insipidus, the Laurence-Moon-Biedl syndrome, pituitary basophilism [Cushing's disease] and obesity as possibly due to hypofunction of the posterior lobe, undersecretion of the fat metabolism hormone of Anselmino and Hoffman or interference with the normal function [hypofunction] of the tuber cinereum. The discussion of the relationship of the hypophysis with the thyroid, the gonads, the parathyroids, the suprarenals and the pancreas, in particular, led to a general discussion of diabetes mellitus and the various etiologic

factors concerned in its appearance. In conclusion, he pointed out that something of the rôle of the "master gland" in the animal economy is just beginning to be understood.)

DISCUSSION

DR. HARRY L. PARKER, Rochester, Minn.: I have listened with much interest to Dr. Luckhardt's handling of this difficult and controversial subject. My principal difficulty has been with the posterior lobe. The anterior lobe is chiefly glandular, and I can see that a great deal can be expected clinically from underfunction and overfunction. The posterior lobe is largely glial. I should like to understand how disturbance of a mere inert glial structure can produce so many symptoms, especially if this is separated completely from the glandular structure in front of it. What does Dr. Luckhardt think is the function of the posterior lobe?

DR. R. L. JENKINS: Recently I studied the case of a child with the Laurence-Moon-Biedl syndrome at the Institute for Juvenile Research. It is not surprising that there is an association in this syndrome between obese body form and underdeveloped genitalia. It is rather surprising to me that this should be associated with polydactylism. It does, however, seem to be so associated; in affected families some children have the full syndrome of Laurence and Biedl and some have merely polydactylism. Has Dr. Luckhardt any explanation for this?

DR. PERCIVAL BAILEY: What has always made me doubt the truth of the things that are said about the posterior lobe of the hypophysis is that I have taken it out many times and no symptoms developed. This has been done by other people also. The syndrome of pituitary basophilism has never been convincing to me. Many observations of adenomas of the cortex of the suprarenal gland associated with similar symptoms have been made, and recently I had several such tumors sent to me for study. In one case there was a small adenoma of the hypophysis, but specific stains proved that there were no basophilic cells in the adenoma.

DR. ARNO B. LUCKHARDT: The thought entertained by some is that the Laurence-Biedl syndrome is a genotypic disease, but I suppose nothing can be definitely stated about its cause until some neurologist makes a careful examination of specimens and tells whether neurologic defects are found in the hypothalamic region.

As regards polydactylism, I mentioned that because both the familial character of the disease and polydactylism are commonly considered to be degenerative changes.

As to what I think about the physiology of the posterior lobe, that was expressed by Dr. Bailey's statements. I know of no function of the posterior lobe. Undoubtedly one can obtain extracts from it that will elevate the blood pressure, having an oxytocic action, and an extract that is useful in the treatment of diabetes insipidus, but that is a pharmacologic action.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, April 26, 1934

A. W. STEARNS, M.D., *Presiding*

POSTENCEPHALITIC PARKINSON'S DISEASE TREATED BY TOTAL THYROIDECTOMY. DR. ABRAHAM MYERSON and DR. DAVID D. BERLIN.

The rationale which prompted one of us (A. M.) to select a patient with Parkinson's disease for total thyroidectomy is as follows: First, in cases of active untreated Parkinson's disease the metabolism is increased, and second, the drugs that are in any way successful in ameliorating the condition of the patient lower the metabolism.

History.—E. C., aged 32, married, had encephalitis at the age of 19. In the next two years she was sleepy, weak and depressed. This condition persisted moderately until about twelve years ago, when she began to notice shaking of the right leg. Gradually the shaking spread to all the limbs, the face and the tongue. The face became stolid, and the patient presented a characteristic Parkinson syndrome. She gave birth to a child in 1927. The symptoms increased, and the condition grew worse despite varied types of treatment; for two months before it was decided to perform a thyroidectomy she was bedridden. The tremor was as marked as in any case we have studied. The churning of the jaws was so great that the saliva became foamy. The patient could not feed herself, and speech was almost indistinguishable. At this time she was receiving eight hypodermic injections of 1/50 grain (0.0013 Gm.) of scopolamine each day, together with varying, but large doses of phenobarbital, amytal and other sedatives. During the period of the illness she had received from various neurologists scopolamine, stramonium, harmine, atropine, parathyroid gland, calcium lactate and belladonna. It is noteworthy that 3 grains (0.19 Gm.) of stramonium leaves three times a day had no effect. Sterile milk was also employed in the latter part of 1930. Typhoid vaccine was tried for a moderately prolonged time. Thus, summarizing the treatment, all forms had been used, and even with the most massive doses of scopolamine and other drugs, the patient became bedridden, and the tremor and rigidity were extreme, the tremor being more noticeable, however, than the rigidity.

Course.—The patient entered the Greater Boston Bickur Cjolim Hospital on June 25, 1929. She was sent to the Beth Israel Hospital on Dec. 5, 1933, where a total ablation of the thyroid gland was done by one of us (D. D. B.) without incident. Prior to the operation the metabolic rate was —29. This we ascribed to the enormous doses of scopolamine which the patient was receiving.

No noticeable improvement occurred during the first two weeks. In fact, when the patient left the hospital her condition was probably somewhat worse than before the operation. About the third week it was noted that her condition was improving. Gradually, as she approached a myxedematous stage, manifested by harshness of the skin and a decreasing metabolic rate, which reached —35, it was possible to control the condition with much less of the drug than before. Some time in the early part of February 1934, the patient was able to get out of bed, walk, raise her hands and hold them outstretched with little tremor. There was some definite tremor around the mouth. She could be kept in this condition with three doses of scopolamine a day and a small doses of phenobarbital. Prior to the operation she had complained of pain in the ankles and feet. This became the most troublesome of her symptoms.

On March 21, 1934, a note stated: "The patient walks with a slight drag of the legs and with a typical parkinsonian facies and lack of associated movements. Speech is clear, although the voice is weak. There is no noticeable tremor of the face. The tongue protrudes straight and is red and without noticeable tremor. There is marked plastic rigidity of the neck. The patient can feed herself. When she raises her arms they are held steady. The grip is fairly firm. There is no swing of tremor to the opposite side when either hand is used, although movements of the hands set up a slight associated tremor of the mouth. The arms are not spastic. The patient feels much better. She does not fall asleep as frequently as formerly, and she is grateful for the results."

The scopolamine was not administered for two days. During this period the patient became markedly worse and, in fact, reached the preoperative stage. She became so tremulous that she could not use her hands. Speech became very indistinct, and the churning of the saliva into foam recurred. When she was again given scopolamine, which is now being administered in two doses of 1/50 grain daily, the symptoms became immediately ameliorated, and she is now ambulatory.

Myxedema was easily controlled by a small dose of thyroid ranging from 1/2 to 3/4 grain (0.033 to 0.048 Gm.), daily. We have not tried the effect of large doses because it seems likely that this would stop the effects of the scopolamine;

that is, it would restore the previous helpless condition. The after-care in this case is difficult, and it is probable that the patient will require constant medical management.

Comment.—We do not in the least expect that this therapy will cure Parkinson's disease, nor do we know that all other patients will react as this one did. The results constitute a valid basis for further work along this line.

DISCUSSION

DR. D. GREGG: Have Dr. Myerson and Dr. Berlin noticed any need to increase the dose of scopolamine during the last two months?

DR. A. MYERSON: The patient is taking two doses a day. She had three doses today because of coming here tonight. She has received as much as eight doses a day and much more before the operation, as well as considerable phenobarbital. She has one very annoying symptom: extreme pain in the heels. I have never observed this in Parkinson's disease before. No surgeon has been able to find what causes it.

DR. G. CLYMER: Did the pain antedate the operation?

DR. D. GREGG: How much thyroid does she receive?

DR. A. MYERSON: The pain did not antedate the operation. The patient is receiving ¾ grain of thyroid a day. Mentality is not impaired. There is no apathy, and memory is good.

DR. E. S. ABBOT: Did the handwriting show a fine tremor?

DR. A. MYERSON: I have not tested the handwriting. The patient has not written for years.

DR. G. CLYMER: Has she any symptoms of myxedema?

DR. A. MYERSON: She was very stout before the operation and always ate well. Lately she has complained of dryness of the skin, and she is myxedematous. This is helped by the thyroid.

DR. H. SOLOMON: That is a small amount of thyroid to cause such a great change.

DR. DONAL SHEEHAN: Has there been any effect on the spasticity?

DR. A. MYERSON: There has been some effect, but more on the tremor.

DR. HALE POWERS: Does this work not suggest that removing the suprarenal glands would produce similar results?

DR. A. MYERSON: The suprarenal glands cannot be supplied artificially. One can substitute for the thyroid. The theory was that the thyroid was pushing the body machinery too hard, and we found that it might work fairly well without the gland.

DR. DAVID D. BERLIN: I became interested in this problem at the invitation of Dr. Myerson and, of course, being a surgeon I know nothing about Parkinson's disease from the neurologist's point of view. One should not expect any real improvement too early, for the benefits derived from this operation depend on the fall in the basal metabolic rate. Between four and six weeks after operation the metabolism should be reasonably depressed, and clinical improvement, therefore, should become manifest.

This patient was in a pitiable condition prior to operation. She was helpless. She shook violently and was cyanotic and frothed at the mouth.

It is known that total thyroidectomy with preservation of the parathyroid glands and recurrent laryngeal nerves is technically possible, for the operation has to date been performed on seventy patients suffering from chronic intractable heart disease. This therapeutic measure was recently evolved at the Beth Israel Hospital in Boston by Blumgart and his co-workers. The same operation was performed on this patient, with removal of every vestige of thyroid tissue but with preservation of the recurrent laryngeal nerves and parathyroid glands. The latter structures are located in the so-called danger zone of the tracheo-esophageal

sulcus, which must be intentionally invaded in the process of ablating all thyroid tissue. Such complete removal of the entire gland is necessary to assure the consistent permanent lowering of the metabolic rate. The severe myxedema which develops can be readily controlled by small doses of thyroid, varying from ¼ to ½ grain daily, the metabolic level usually remaining between —25 and —30 per cent, and the distressing symptoms of myxedema being relieved.

The recurrent laryngeal nerves constitute by far the greatest technical hazard in this operation. Since we have found it necessary to expose these nerves in 61 per cent of our operations for heart disease, the danger of bilateral injury by ligature or section is imminent, and caution must be exercised. We are not especially concerned about the parathyroid glands, since it is not difficult to preserve two, or at least one, a number sufficient to protect the patient against the development of tetany. Fortunately, the parathyroid glands are not infrequently tucked away from the zone of the operation beyond operative injury.

DR. J. J. THOMAS: The Parkinson symptoms came on slowly and gradually, and when I last saw the patient she was not helpless and her condition was well controlled by the use of scopolamine. One must congratulate Dr. Myerson on the remarkable improvement he has produced in this patient, and all the members will watch with interest further experience with this method.

EXTENSIVE INTRACEREBRAL CALCIFICATION. DR. J. KASANIN and DR. R. P. CRANK, State Hospital for Mental Diseases, Howard, Rhode Island.

This article will appear in full in a later issue of the ARCHIVES.

TUBEROUS SCLEROSIS WITH UNUSUAL BONY LESIONS. DR. JACQUES S. GOTTLIEB and DR. GEORGE R. LAVINE.

This article appears in full in this issue, page 379.

PHILADELPHIA NEUROLOGICAL SOCIETY

April 27, 1934

D. J. McCARTHY, M.D., *President, in the Chair*

TUMORS OF RATHKE'S CLEFT (HITHERTO CALLED TUMORS OF RATHKE'S POUCH). DR. CHARLES H. FRAZIER and DR. BERNARD J. ALPERS.

This article was published in full in the November 1934 issue of the ARCHIVES, page 973.

LOCALIZATION OF THE MECHANISM CONTROLLING SLEEP. DR. STUART N. ROWE.

In a survey of the literature dealing with lesions of the diencephalon associated with disturbances of sleep, relatively few reports presenting the exact location of the pathologic process could be found. Accordingly, this material was critically reviewed, and 3 cases of tumor of the interbrain (2 associated with marked hypersomnolence and 1 with no change in the normal sleep rhythm) were studied by serial sections in an effort to contribute to the more exact localization of the cerebral mechanism controlling sleep. The rather wide disagreement among previous writers on the subject may be due to the many difficulties and sources of error involved, such as: (1) the confusion of stupor with true hypersomnolence, (2) incomplete pathologic study, (3) the frequent occurrence of widespread pathologic changes and (4) the difficulties of interpreting results in animal experimentation. In general, the most reliable evidence at hand seems to favor four possible locations in the diencephalon of the mechanism controlling sleep: (1) the tubo-

infundibular region, (2) the periventricular gray matter, (3) the medial portion of the thalamus and (4) the gray matter surrounding the cephalic portion of the aqueduct.

In 2 of the cases of diencephalic tumor associated with hypersomnolence the lesion occupied the dorsal and posterior portions of the interbrain, involving the thalamus bilaterally in one instance and unilaterally in the other and chiefly the medial thalamic nuclei. The periventricular gray matter on both sides of the third ventricle was infiltrated, including the nucleus reuniens and the nucleus paraventricularis. The lesions did not disturb the infundibular and tuberal regions (including the supra-optic and the tuberian nuclei of the hypothalamus) and did not extend far into the mesencephalon. In the third case, in which no disturbance of sleep occurred, the tumor invaded only one side of the diencephalon, occupying almost the entire thalamus. This lesion extended more ventrally (down to the mamillary bodies) and farther caudally into the midbrain than did the others.

From this material it seems that bilateral involvement of the periventricular gray matter of the third ventricle and probably at least unilateral thalamic damage are necessary to produce the symptom of hypersomnolence.

DISCUSSION

Dr. William G. Spiller: Dr. Rowe has given a fair presentation of the chief factors concerned in the production of sleep. Weisz, considering the syndrome presented by Stertz, studied clinically and pathologically 6 cases of tumor of the interbrain. He concluded that, in addition to the location of the lesion, its intensity and rapidity of development have much to do with causing symptoms referable to the interbrain. No typical anatomic location of the lesions producing the symptoms was discovered in his cases. The lesions were widely distributed about the third ventricle. Lesions were found also in the cerebral hemisphere opposite to that containing the tumor and were of vascular origin. He concluded that the same clinical effects may be produced from different parts of this area. Somnolence especially predominated in the clinical picture.

Pette emphasized that the same symptomatology in different cases may be caused by lesions of different locations and different degrees of severity.

Foerster remarked that an extended area in the brain stem is concerned with the control of vegetative functions. It extends from the lamina terminalis through the area of the third ventricle, the central gray matter of the aqueduct, the tegmentum of the pons and the medulla oblongata to the obex of the fourth ventricle. Sharply distinguishable centers for the separate vegetative functions do not exist in this extensive area, although there are certain special areas from which certain vegetative symptoms may be produced. In illustration, acute symptoms referable to the medulla oblongata are thirst, fatigue, somnolence or loss of consciousness, slowing of the pulse, forced breathing and later respiratory paralysis. From the anterior part of this area psychic symptoms may be produced, even of extreme degree; from here may arise also the high temperature, polyuria and polydipsia. The most dangerous area in which lesions give rise to respiratory failure is that of the corpora quadrigemina; the slightest pressure here may cause instant arrest of the respiratory function.

Weisz suggested that the term "centers" should not be used in reference to the area under consideration.

Burger-Prinz, in a paper devoted to the study of sleep, in describing diencephalic symptoms, mentioned somnolence especially. He reported four cases of tumor in or about the third ventricle in which somnolence was prominent with other symptoms. Such cases as these in connection with those of Weisz do not permit the sharp localization and limitation of a sleep center.

All of Burger-Prinz' patients lacked initiative and activity. The sleep lasted hours, days or weeks; sometimes it was interrupted by wakeful periods lasting days. Such sleep may more nearly resemble stupor. There may be no dream state. The awakening may be without the sensation of renewed vigor. Sleep depends on many causes, such as endocrine processes, metabolism, intestinal activity

and mental function. Pathologic sleep is not the same as normal sleep, as many have learned from the study of epidemic encephalitis. The mechanism of sleep is not understood; it is not known whether it is a process of inhibition or of excitation.

DR. E. A. SPIEGEL: So little is known about the central mechanism that regulates the periodic alteration of the waking and sleeping states that every careful observation is highly welcome, particularly if it is so well presented as this one has been by Dr. Rowe. The cases of Dr. Rowe have interested me particularly in view of the recent experiments of Dr. Ranson. This author injured the brain stem between the mamillary body and the third nerve in the region where Economo postulated a sleep center. He observed somnolence in the animals so treated combined with a peculiar state of catalepsy, so that this condition was comparable with some cases of encephalitis. It was supposed by Economo and his followers that this sleep center acts by inhibiting the central mechanisms which have to do with consciousness, including the cerebral cortex. If one assumes that a certain center is able to perform such an inhibition, one should be able to show that pathways arise from this center leading to the ganglia to be inhibited. It has, however, been already pointed out by Troemner that such pathways from the periventricular gray matter to the cerebral cortex have never been demonstrated. On the other hand, the thalamus has rich connections with the cerebral cortex. Hence a simple anatomic consideration makes it rather impossible that the hypothetic sleep center exists in the paraventricular gray matter. If somnolence can be produced by lesions of the paraventricular gray matter, there may be several reasons for it. A functional relationship may exist between the paraventricular nuclei and the optic thalamus. It is also possible that lesions anatomically limited to the periventricular gray matter produce irritative phenomena in the neighboring medial parts of the thalamus. I believe, therefore, that there is so far no exact proof of the existence of a sleep center in the periventricular gray matter. If diseases of the posterior part of the diencephalon cause sleep to occur, it seems that this is due to the injury of the optic thalamus more than to involvement of a sleep center in the paraventricular gray matter. Dr. Rowe is therefore right in concluding that periventricular lesions must be combined with at least unilateral thalamic damage in order to produce hypersomnolence.

EXPERIMENTAL INTESTINAL ULCERATION FOLLOWING SUPRARENAL DAMAGE. DR. CHARLES W. MCLAUGHLIN.

This article will be published elsewhere.

NEUROGENIC ORIGIN OF DUODENAL ULCER: REPORT OF TWO CASES. DR. FRANCIS C. GRANT.

Cushing (*Surg., Gynec. & Obst.* **55**:1, 1932) has reported 11 cases of intracranial lesions accompanied by a gastric lesion. In 6 of the cases a tumor lay in the cerebellum; in 5 of these the growth involved the vermis and the roof of the fourth ventricle, while in the sixth a large basilar aneurysm lay anterior to the brain stem. Acute erosions developed in 5 of these cases, resulting in perforation of the viscus. In the sixth case, in which the presence of a midline cerebellar tumor was verified, the patient, a child, lived for two years and at autopsy a chronic duodenal ulcer was found. In 2 cases of cerebral tumor, 1 of meningioma of the olfactory groove and 1 of hypernephroma metastasizing to the right parietal lobe from the left kidney, acute gastric erosions with hematemesis were a contributing cause of death. Of 2 cases of malignant hypertension, a sudden abdominal crisis developed in 1, and laparotomy was performed with closure of a ruptured gastric ulcer, while in the other the patient died abruptly with hyperthermia and autopsy revealed multiple recent gastric ulcers. In the eleventh case there was a third ventricular tumor which was verified by a ventriculogram; the tumor proved to be radiosensitive, and the patient was benefited by roentgen therapy; later, he reappeared with gastric symptoms, and roentgen studies of the gastro-

intestinal tract revealed unmistakable evidence of a gastric ulcer. In the course of a second series of roentgen therapy for the tumor of the brain all symptoms of the duodenal ulcer disappeared.

Within the last year 2 cases of verified midline cerebellar tumor, 1 of ependymoma and 1 of spongioblastoma unipolare, have been seen in the neurosurgical department of the University Hospital. In 1 case following apparently successful surgical treatment, when the child was considered well on the road to recovery, symptoms of gastro-intestinal bleeding occurred which eventually led to death. These cases are reported because of the circumscribed nature of the lesion in 1 instance and the further evidence thus established of the control of diencephalic centers over the proper functioning of the gastroduodenal mechanism.

CASE 1.—R. C., a white boy aged 10 years, was apparently well until a year before examination, when blurred vision developed. During the past year the visual loss gradually increased, and the boy had headaches and vomited every week or two. Twice, dizzy spells caused him to fall down without apparent cause. Slight mental retardation was noted.

There were no gastro-intestinal disturbances up to the time of the onset of the present symptoms. Physical examination showed a normal-appearing boy with a large head, 58 cm. in diameter. A normal measurement for this age is 51 cm. Vision was poor in both eyes. There were bilateral choked disk, (from 3 to 4 diopters), slight dysdiadokokinesia, dysmetria and moderate hypotonia in all extremities, pendulous knee jerks bilaterally and a cracked pot sound on percussion over the skull.

The blood count was normal; urinalysis gave negative results and the Wassermann reaction was negative. The visual fields showed left homonymous scotomas.

On March 15, 1933, Dr. Grant performed suboccipital craniectomy. On retracting the cerebellar tonsils over the lower end of the fourth ventricle, what was supposed to be a tumor in that region was encountered, so that a section through the vermis was made. Prior to the section of the vermis, 1.5 cc. of indigo carmine had been injected into the right lateral ventricle. None of the fluid appearing from the fourth ventricle was tinted with the dye. Exposure through the vermis showed the entire fourth ventricle but failed to expose the tumor. The fourth ventricle did not seem to be dilated. A good view of the aqueduct was obtained, and because no fluid was passing through it the eye of a small probe was passed up through the aqueduct. This allowed the immediate escape of 4 or 5 cc. of deep blue fluid. A small bayonet forceps was then passed closed through the orifice and allowed to open in it. This was followed by the escape of 10 or 15 cc. more of bluish fluid. The aqueduct was dilated in this way in the 12 and 6 o'clock planes and in the 9 and 3 o'clock planes. This was followed by a free flow of fluid. On passing the forceps through the aqueduct there was nothing to suggest that the patient had a tumor of the third ventricle. Clinically, no evidence existed of the presence of a tumor in the neighborhood of the pineal gland. Since, for the time being at least, circulation of the cerebrospinal fluid had been restored, hemostasis was completed and the wound was closed in layers as usual without drainage.

The child's condition following operation was very poor, and he was given two transfusions of 200 cc. each. Seventy-two hours after the operation he began to have tarry bowel movements. These continued with increasing frequency until he died on March 22, at 6:35 a. m. on the seventh postoperative day. Transfusions of 250 cc. each were given on March 21. In the last stages the temperature was 107 F., the pulse rate 160 and the respiratory rate from 40 to 50.

Postmortem examination of the brain showed marked hydrocephalus of all ventricles except the fourth, which was moderately dilated. The dilatation of the ventricular system was equal on the two sides. The pineal gland measured 4 mm. in diameter and was cystic. The center contained yellow fluid. It did not appear to be tumorous.

The aqueduct of Sylvius had apparently been occluded before operation. This was evidenced by a questionable proliferation of the ependymal cells, which had formed an obstruction to the flow of fluid.

The transverse intercollicular groove was completely lacking. The left colliculus was one third again as large as the right. In transverse section the enlargement of the left colliculus seemed to be due to a round, white, hard tissue which was not definitely outlined. The same condition existed on the right side. These masses located in the colliculi extended medially to compress the aqueduct and inferiorly to a short distance below the level of the aqueduct. They had no distinct outline. They were avascular, white and extremely tough.

Microscopically, the iter was practically occluded; only a narrow, slitlike space remained of the aqueduct. Around it was a neoplastic process which involved the tissues around the iter and spread up and down in the midline.

Within this area were ependyma-like pockets which were probably normal and represented out-pouching of the iter. The tissue around the iter was quite cellular, with the cells running in many different directions. There were streams of cells visible and others cut in cross-section. Around the iter the cells had a radial appearance, but this was lost farther away. The cell nuclei were large, oval, elongated and often indented. The cytoplasm was frequently arranged in polar fashion, with a stout polar process. Occasional astrocytes were seen. Among the cells were many stout fibrils, some of which were connected with the cells. The colliculus of one side was invaded by tumor. The diagnosis was spongioblastoma unipolare.

The stomach was normal in size, shape and thickness. The mucosa was somewhat smoother than normal as a result of autolysis. It was pale pink with a few tiny dilated venules visible over the crests of the rugae. The pylorus was normal. There was a few cubic centimeters of colorless mucoid fluid in the lumen.

The wall of the duodenum was of the usual thickness. The mucosa was a rather dark pink with numerous tiny dilated venules visible in its depths. About 2 cm. below the pylorus on the posterior wall of the duodenum, where the pancreas was adherent to it, there was a shallow ulcer, about 1 cm. in diameter. The base of the ulcer was covered by a thin layer of tenacious dark yellow mucus which was scraped off with difficulty, leaving a light pink granular surface in the center of which was a tiny pit, about 1 mm. in diameter and 0.5 mm. in depth. The edges of this ulcer were low and soft, with no palpable induration or visible discoloration. The lumen of the duodenum contained a small amount of light yellow chyme.

The jejunum, ileum, colon and suprarenal glands were normal.

CASE 2.—M. F. was admitted to the University Hospital on May 15, 1933, with the complaint of headache and vomiting; the vision in the left eye was impaired. There were no gastro-intestinal symptoms until the onset of the present illness. Neurologic examination showed a Romberg sign, dysmetria with the left hand, palsy of the right lateral rectus muscle, choked disks of 4 diopters, a sluggish right pupil and generalized areflexia.

There was roentgen evidence of increased intracranial pressure and convolutional atrophy.

A ventriculogram on May 29 showed bilaterally dilated lateral ventricles and a dilated third ventricle without a shift to the midline, pointing to a cerebellar lesion.

Suboccipital craniectomy on May 29 showed a midline cerebellar tumor, which proved to be an ependymoma.

Convalescence was uneventful, and the patient was discharged on June 13 with little bulging at the site of the decompression. The patient remained free from symptoms until August, when the headache and vomiting returned.

At the second admission (September 5) neurologic and physical examinations gave the same results as at the first admission.

Dr. Grant performed a suboccipital craniectomy on September 15, and an ependymoma involving the vermis and extending down into the fourth ventricle and into the right cerebellar hemisphere was exposed and radically removed.

Progress was good until September 23, when the patient passed a grossly bloody stool. On advice of the surgical consultant the condition was treated as

for bleeding ulcer. Small daily transfusions were given, but the stools continued to be tarry and loose with frank blood clots. An intravenous drip (5 per cent dextrose) was started September 26. The patient died on September 27.

Postmortem examination of the brain showed it to be edematous. There was a moderate degree of internal hydrocephalus, which was greater in the inferior than in the anterior or posterior horn of the lateral ventricle. The third ventricle and iter were dilated. The brain showed active postmortem changes, with the typical Swiss cheese appearance of the brain.

Filling the fourth ventricle was a tumor which was firmly adherent to the floor of the medulla and seemed to extend into the right cerebellar hemisphere. Despite the removal of a large piece of tumor, the ventricle still seemed entirely filled with the neoplasm. The tumor had a reddish fleshy appearance and seemed to infiltrate the floor of the fourth ventricle. It could not be pulled away from it. The left cerebellar hemisphere and vermis did not seem to be invaded.

In the peritoneal cavity was about 500 cc. of dark brown, foul-smelling fluid, which had a distinctly bloody appearance in the right upper quadrant, where close examination revealed extensive necrosis of the jejunum, mesentery and omentum. The necrosis was obviously due to digestion by gastric fluid leaking from a large perforation in the first portion of the duodenum. The jejunum was completely destroyed in some areas, the lumen communicating with the abdominal cavity through ragged openings. The gastrohepatic ligament was partly destroyed. There was a zone of discoloration, about 3 cm. in width, over the dome of the liver where the gastric fluid had seeped between the liver and the diaphragm. The undersurface of the diaphragm was markedly digested and was completely destroyed in several small areas. The colon and ileum were dusky purple owing to blood in the lumen. The stomach and the portion of the bowel above the jejunal erosions were pale and collapsed.

The wall of the stomach was of normal thickness and of good tone. The mucosa was pale and velvety and was thrown into pronounced rugae. The lumen contained large quantities of mucus and a small amount of partly digested blood.

In the duodenum, just below the pylorus, was a deep irregular ulcer with flat edges. This ulcer lay on the upper and posterior aspects of the first portion of the duodenum and measured about 1 by 2 cm. There was a large gaping perforation, about 0.8 cm. in diameter, in the upper aspect of the ulcer which communicated freely with the peritoneal cavity. There were no adhesions to surrounding structures. The lumen of the duodenum was empty except for a little clear mucus and a few flecks of partly digested blood. The mucosa below the ulcer was pale and velvety.

The upper portion of the jejunum was of normal size and thickness, and the mucosa was normal. At the lower portion of the jejunum were numerous irregular areas of necrosis, with complete destruction of the wall in places. The mesentery in these regions was partly or completely digested. The necrotic areas in the bowel allowed free communication between the lumen and the peritoneal cavity. These lesions were obviously the result of digestive action from without rather than from within the intestine.

The entire bowel below the necrotic areas was filled with clotted and partly digested blood. The mucosa was stained by blood but showed no other lesion.

The lumen of the colon was filled with partly digested blood. The mucosa was blood-stained but otherwise was normal.

The suprarenal glands were entirely normal on gross examination.

Microscopic examination of the stomach showed the muscularis to be of normal thickness. The mucosa was well preserved and showed no lesion. The section from the edge of the ulcer in the duodenum showed it to extend cleanly through all the coats as though punched out. There was a slight degree of leukocytic infiltration in the adjacent tissue but no fibrosis.

Comment.—These 2 cases correspond closely with those described by Cushing. However, the lesions of the brain are dissimilar in type and in character, although the effect on the gastroduodenal region was much the same. That either of these

duodenal ulcers could have been produced by agonal or postmortem changes is unlikely, because blood appeared in the stools seventy-two and ninety-six hours ante mortem. Furthermore, at autopsy there was no evidence of autodigestion of the stomach or the duodenum in either case. In one brain a circumscribed lesion surrounded the iter and involved both colliculi. In the other, neither of these areas was implicated, the tumor appearing in the roof and sides of the fourth ventricle and adjacent portion of the cerebellum. The lesion in the colliculi might conceivably have involved directly the posterior hypothalamic nuclei controlling the sympathetic and parasympathetic nuclei, the tumor in the roof and sides of the fourth ventricle and efferent fibers running from these centers. In one instance the centers seemed to have been damaged, and in the other, their efferent pathways.

EFFECT OF LESIONS OF THE HYPOTHALAMUS ON THE GASTRO-INTESTINAL TRACT AND HEART IN MONKEYS. DR. JAMES W. WATTS, Philadelphia, and DR. JOHN F. FULTON, New Haven, Conn.

Eighty autopsies were performed on monkeys, 17 of which were in animals with diencephalic lesions. A clip was placed on the pituitary stalk in 2 animals, and some portion of the hypothalamus was destroyed in 15. The monkeys with hypothalamic lesions were killed at various intervals after operation, and the gastro-intestinal tract was carefully examined. Suspicious-looking areas from the alimentary canal were taken for microscopic study, and serial sections of the diencephalon were cut to determine the extent of the lesion. The majority of the remaining 63 postmortem examinations were on animals which had undergone operations on some other part of the brain or the spinal cord.

The experiments indicate no relationship between the destruction of any single group of hypothalamic nuclei (supra-optic, tuberian or paraventricular) and the pathologic changes in the gastro-intestinal tract. However, a study of the serial sections of the diencephalon show that a large hypothalamic lesion was present in every animal, except 1, in which erosions of the alimentary canal were present. The postoperative condition of most of the animals having erosions was very grave; 3 died, 1 was killed because death was expected within twenty-four hours, and 1 was in good condition when killed. Only 1 animal not subjected to hypothalamic lesion had mucosal erosions. This monkey, which had received repeated injections of ephedrine following a transection of the spinal cord in the midthoracic region, died from meningitis in a state of emaciation.

Although anorexia and the poor general condition of the animal may predispose to the development of pathologic changes in the alimentary tract, it should be borne in mind that the symptoms followed large hypothalamic lesions so often that they may be looked on as part of the syndrome due to destruction of this area. Also, it must not be overlooked that numerous monkeys in the control series died following operations on other parts of the brain without showing such changes in the intestine.

It appears that large lesions in any part of the hypothalamus in monkeys may result in mucosal erosions or even perforation of the upper portion of the gastro-intestinal tract. However, only 1 chronic peptic ulcer was encountered in the series of 80 autopsies, and this was in an animal that had not been operated on.

Bleeding into the lumen of the alimentary tract was observed in 5 instances: twice in animals with hypothalamic lesions, once in a monkey with both premotor areas removed and twice in animals into which ephedrine had been injected following transection of the spinal cord in the midthoracic region. Punctate and focal mucosal hemorrhages were seen as often in the control series as in the animals with hypothalamic lesions.

News and Comment

SECOND INTERNATIONAL NEUROLOGICAL CONGRESS

Further plans for the Second International Neurological Congress have been made by the local committee in London. The morning and afternoon sessions devoted to the epilepsies, under the direction of Professors Marburg and Rossi, will occupy the first day of the congress, Monday, July 29. The program is as follows:

1. General Etiology of Epilepsy. Prof. Dr. J. Abadie, Bordeaux, France.
2. Special Etiology of Epilepsy. Prof. Dr. V. M. Buscaino, Catania, Sicily.
3. Experimental Pathogenesis of Epilepsy. Dr. Stanley Cobb, Boston.
4. Chemical Pathogenesis of Epilepsy. Dr. Frisch, Austria.
5. The Vegetative Nervous System in Relation to Pathogenesis. Prof. Dr. K. Orzechowski, Warsaw, Poland.
6. Pathologic Anatomy of Epilepsy. Prof. Dr. W. Spielmeyer, Munich, Germany.
7. Medical Therapy. Dr. Ulrich, Switzerland.
8. Surgical Therapy. Dr. Wilder Penfield, Montreal, Canada.
9. Roentgen Therapy. Dr. M. Sgalitzer, Vienna, Austria.
10. Institutional and General Treatment. Dr. L. J. J. Muskens, Amsterdam, Holland.

On Tuesday morning the following program on the physiology and pathology of the cerebrospinal fluid, prepared by Professor Foerster, will be given at 9:30 a. m.

1. Physiology of Secretion and Resorption of the Cerebrospinal Fluid. Dr. Lewis H. Weed, Baltimore.
2. Physiology of Secretion and Resorption and Its Anatomical Basis. Dr. G. Schaltenbrand, Hamburg, Germany.
3. Pathology of Secretion and Resorption. Dr. Riser, Toulouse, France.
4. Therapeutic Procedures Against Disturbances of Secretion and Resorption. Mr. Hugh Cairns, London, England.
5. Physiochemical Basis of Secretion and Resorption. Dr. Georgi, Gverdon.

On Thursday morning, August 1, the following program on the functions of the frontal lobes, prepared by Professor Claude, will be presented:

1. The Relation of the Functions of the Frontal Lobes to Manifestations of Cerebellar or Labyrinthine Type. Prof. J. A. Barré, Strasbourg, France, and Prof. Dr. P. Delmas-Marsalet, Bordeaux, France.
2. The Relations Between the Frontal Lobes and Motor Functions. Prof. Dr. Kurt Goldstein.
3. The Relations of the Frontal Lobes with the Pyramidal System. Prof. Dr. A. Donaggio, Modena, Italy.
4. Modifications of Function Observed After Surgical Intervention on the Frontal Lobes. Dr. Clovis Vincent, Paris, France.

A consideration of the hypothalamus and the central representation of the autonomic system under the chairmanship of Professor Brouwer will be held on Friday, August 2, at 9:30 a. m.

1. Phylogenetic Development. Prof. Dr. C. U. Äriens Kappers, Amsterdam, Holland.
2. The Ontogenetic Development and Normal Conditions in Man. Prof. Le Gros Clark, Oxford, England.
3. Physiology. Prof. Dr. W. R. Hess, Zurich, Switzerland.
4. Clinical and Pathological Aspects. Prof. Dr. J. Lhermitte, Paris, France.
5. Surgery. Dr. Harvey Cushing, New Haven, Conn.

The afternoon sessions for miscellaneous subjects will begin at 2 p. m. and will be held Tuesday, Thursday and Friday afternoons. Miscellaneous papers will be presented at these sessions grouped under appropriate headings. The symposiums will be held in the large hall of University College, Gower Street, W. C. 1, and the miscellaneous sessions will be held in the smaller lecture rooms of the college.

The official reception for all members of the congress will be held on Monday evening at 9 p. m., the exact place of the reception not yet being determined. On Tuesday, July 30, at 9 p. m., there will be a reception by the president and Fellows of the Royal College of Physicians at their college, Pall Mall, S. W. 1, and by the president and Fellows of the Royal College of Surgeons at their college, Lincoln's Inn Fields, W. C. 2. On Thursday, August 1, at 7:30 p. m., the official banquet of the congress will be given at Grosvenor House, Park Lane, W. 1. On Friday evening, August 2, at 8:30 p. m., the triennial Hughlings Jackson memorial lecture will be presented by Prof. Otfrid Foerster. All members of the congress are cordially invited to attend this lecture. A reception will be held by the Section of Neurology of the Royal Society of Medicine following the conclusion of the lecture.

The S. S. *Manhattan* of the United States Lines has been selected as the official steamer for the American delegation to the congress. It will sail from New York at noon on July 17 and is due to arrive at Plymouth, England, on July 23. Since the opening date of the congress is July 29, the intervening time is available for travel in England. Any steamer of the United States Lines is available for the return voyage to New York after the congress, and there are frequent sailings from French, English and Irish ports.

The S. S. *Manhattan* carries cabin class and tourist class passengers. The minimum cabin class rate from New York to Plymouth, on a basis of half-round trip is $154.50. Minimum tourist class passage on the same boat is $102. For west-bound passage, on the same basis, the minimum cabin class fares range from $116.50 on the S. S. *President Harding* or S. S. *President Roosevelt* to $154.50 on the S. S. *Manhattan* or S. S. *Washington*. After August 11, the west-bound fares are somewhat higher. The S. S. *Washington* carries cabin class and tourist class passengers, while the S. S. *President Roosevelt* and S. S. *President Harding* carry only cabin class passengers.

The official travel agents, Thomas Cook and Son-Wagons-Lits, Inc., suggest and offer an inclusive tour, with a continental extension, an outline of which is given here. Inclusive prices are available on application.

A number of hotels in London are recommended, and the "Metropole" is especially suggested for American members because of its location and facilities. The official travel agents will gladly make reservations at this or any other hotel on request.

A variety of half day and day sightseeing excursions to and around London will be available during the period of the congress and especially on Wednesday, July 31, on which day no meetings are scheduled. These excursions will include London, Hampton Court, Windsor, Eton, Oxford, Cambridge, the Shakespeare Country and the River Thames.

A booklet detailing the travel arrangements for both the ocean crossings and on land is in the course of preparation and will be sent on request to the official travel agents or the American secretary.

Official Main Tour

July 17: Sail from New York on the S. S. *Manhattan* of the United States Line.
July 23: Call at Cobb, Ireland. Arrive at Plymouth, England. By motor, via Truro and Falmouth, to Penzance, for the night.
July 24: By motor, via Land's End and St. Ives, to Newquay, for the night.
July 25: By motor, via Tintagel, Clovelly, Bideford and Barnstaple, to Lynton, for the night.

July 26: By motor, via Minehead, Glastonbury and Wells, to Bath, for the night.
July 27: By motor, via Chippenham, Cirencester and Henley to London.
July 28: In London, at leisure.
July 29 to August 2: In London, attending the congress.
August 3: To Brussels, by rail and Channel steamer via Dover and Ostend. City sightseeing drive.
August 4: At Brussels. Visit the International Exhibition in the morning. To Paris by late afternoon train.
August 5 to 7: At Paris. One day sightseeing drive; one day motor trip to Versailles and Malmaison; one day at leisure.
August 8: To Havre by train, and sail on the S. S. *President Harding* of the United States Lines.
August 16: Due in New York.

Official Extension Tour

July 17 to August 7: With the main tour.
August 8: To Lucerne by day train. Excursion by steamer to Brunnen and by mountain railway to Axenstein.
August 9: The Grand Alpine Tour by motor via the Furka and Grissel Passes and the Rhone Glacier to Interlaken.
August 10: At Interlaken. Excursion to Lauterbrunnen and Murren.
August 11: By morning train over the Loetschberg-Simplon route to Stresa; by steamer across Lake Maggiore; by mountain railway and steamer to Lugano.
August 12: At Lugano. To Milan by afternoon train.
August 13: At Milan. Morning sightseeing drive.
August 14: To Venice by morning train.
August 15 and 16: Day's sightseeing including the Lido.
August 17: To Genoa by day train.
August 18: To Nice by motor.
August 19: At Nice. By motor over the Corniche Drive to Mentone and Monte Carlo and return.
August 20: To Avignon by morning train. Afternoon sightseeing.
August 21: To Paris by day train.
August 22: To Havre and sail on the S. S. *President Roosevelt* of the United States Lines.
August 30: Due at New York.

According to the latest regulations of the British Committee, the time limit for the submission of titles and abstracts has been extended and the Committee for the United States will accept titles and abstracts up to March 1. Abstracts for the program should not exceed 200 words. Papers can be presented before the congress in English, French, German, Italian or Spanish, but the titles and abstracts must be prepared in either English, French or German. Ten minutes is allowed for the presentation of each paper on the miscellaneous programs.

There are two types of membership—active and associate. Active members consist of all neurologists, neurosurgeons, psychiatrists, and physicians or surgeons interested in neurology. The membership fee for active members is the equivalent of 25 Swiss francs. Associate members are nonprofessional persons, men or women, who are interested in the congress. The fee for associate members is the equivalent of 12½ Swiss francs payable in dollars at the current rate of exchange to the secretary for the Committee for the United States. Applications for both active and associate membership should be made to the secretary of the Committee for the United States. Titles of papers to be presented, together with abstracts, must be in the hands of the secretary of the Committee from the United States before March 1 to receive consideration for inclusion in the program.

The personnel of the Committee from the United States has been changed; the committee appointed by the Council of the American Neurological Association at its recent meeting is as follows: B. Sachs, Chairman; Henry Alsop Riley, Secretary, 117 East Seventy-Second Street, New York; James B. Ayer; Williams B. Cadwalader; Harvey Cushing; George W. Hall, and Colin K. Russel.

Book Reviews

Dementia Praecox—A Psychological Study. By Harriet Babcock, Ph.D. Price, $3. Pp. 168. Lancaster, Pa.: Science Press Printing Co., 1933.

The many complex problems of the condition called dementia praecox have at last been solved! All obscurity has been dispelled at a single stroke, for, in the words of the author, "the characteristics of praecox patients are readily understood when their mental inefficiency is taken into consideration" (p. 101). Dr. Babcock has done a painstaking and stimulating piece of work, and there can be no quarreling with her extremely interesting data. These, however, seem scarcely to warrant the sweeping conclusions, namely, that the phenomena of dementia praecox are similar to those found in diseases admittedly due to organic deterioration, and that such deterioration, and that alone, explains all the phenomena of dementia praecox.

The study consists of a comparison of the mental efficiency of 216 nonpsychotic subjects with that of 206 patients whose conditions were diagnosed as dementia praecox in the Manhattan State Hospital. The mental efficiency was measured by a battery of tests designed to discover the subject's retentiveness and recall and the speed of his mental processes. The level of abstract intelligence is recorded in terms of vocabulary rating. The discrepancy between a subject's level of abstract intelligence and his present mental efficiency is called the "efficiency index" (E. I.). This is not to be confused with mental deficiency, as a subject with a mental age of, say, 6 years in both fields would have a normal efficiency index.

The efficiency indexes of the nonpsychotic group ranged from minus 3.4 years to plus 3.2 years, and for more than three fourths of these subjects the index was above minus 1 year. In the 124 patients with dementia praecox who were cooperative enough to give reliable vocabularies the index ranged from minus 13.1 to plus 0.5 years, with a medium of minus 3.5 years. The efficiency was directly proportional to the degree of social adaptability, as the median inefficiency of the nonparole group was minus 3.8 years, of the group paroled from closed wards minus 2.3 years and of the group paroled from open wards minus 1.6 years. The more detailed data (p. 55) show that "even praecox patients who seem normal 'except for their history' and who show no marked signs of abnormality may be differentiated from normal subjects by the clearness and duration of first impressions, which tend to be even better than normal; by abnormally defective learning ability; by initial slowness in apprehending new ideas, even when they concern familiar data; and by a general slowing of all mental processes which is particularly apparent in any continuous work even when it is very easy to understand and do." This is precisely the kind of defect which the author has found in obviously deteriorated patients with dementia praecox and in patients with dementia paralytica.

In the examinable group, the school histories showed that 37 were two or more years below the normal grade for their mental level; 16 were one year below, and 41 were up to or beyond the expected grade. The author seems to conclude from these figures that the mental inefficiency of these patients was manifesting itself in school many years before the onset of the psychotic manifestations, but she presents no figures for the school history of the normal control group.

The statistical study is closed with an account of the minor differences in amount and kind of mental inefficiency in the four types of dementia praecox. There is a final chapter of summary and conclusions, which seems almost superfluous in view of the liberal interlarding of the whole text with argument. The generally argumentative tone and almost acrimonious denunciation of the whole psychogenic approach to dementia praecox fail to make the conclusions convincing.

The facts presented by the author bring forcibly to one's attention that deterioration begins early in dementia praecox and persists in some degree during remissions. What has been sometimes ignored but often suspected is now proved by quantitative measurements. These facts further emphasize the unreliability of the intelligence test as a whole, and the necessity of further testing and evaluation of psychologic

profiles. They fail to prove that the deterioration is the cause and not a result of the disease or that the psychogenic approach should be relegated to the scrap-heap.

Histopathology of the Peripheral and Central Nervous System. By George B. Hassin, M.D. Price, $6. Pp. 491. Baltimore: William Wood & Company, 1933.

This book of four hundred and ninety-one pages is the result of Professor Hassin's twenty years of personal work on the histopathology of the nervous system plus a great deal of reading in many languages. It is a book for mature students of neurology and psychiatry, not for beginners, for the material is discussed almost entirely from the microscopic standpoint, with little generalization or clinical correlation. Part 1 takes up the diseases of the peripheral nerves; part 2, diseases of the spinal cord; part 3, diseases of the brain, and part 4, staining methods. Under each heading the histopathology of many common and rare diseases is described. The reader can find an adequate presentation of almost any neurologic syndrome and of a few psychiatric syndromes. Thus, it makes a good reference book for clinic or laboratory. The purpose of the book is to describe these diseases "from a histopathologic angle only;" this purpose is well attained. In places the narrow microscopic point of view leads to classifications that seem odd to the clinician; for example, the statement is made that subacute combined degeneration of the cord is similar to Friedreich's disease (page 95).

The author's wide reading has added greatly to the value of the book, and the text is well documented. Occasionally, the author generalizes and argues as to disease processes from the postmortem appearances. It is then that his views can most successfully be challenged. Few neuropathologists will accept his views on the pathogenesis of tabes dorsalis, hydrocephalus and cerebral hemorrhage. Nevertheless, the book is more interesting for being colored by a strong personal point of view forcefully expressed. It is, on the whole, well written, and is excellently illustrated, largely from the author's own specimens. A stickler for good English would be troubled by the frequent use of colloquialisms such as "most likely," and any reviewer would be shocked by "choreatic" for "choreic" and "athetosic" for "athetoid."

Mental Healers. By Stefan Zweig. Price, $3.50. Pp. 363. New York: Viking Press, Inc., 1932.

It is not often that a layman can appreciate the intricate problems involved in psychotherapy and the quest which the best medical minds have made for centuries to understand what takes place in a therapeutic relationship. It still is not known why patients get better and how diverse technics produce exactly the same results.

Zweig discusses the biographies of Mesmer, Eddy and Freud. The first is by far the most interesting and the most penetrating and gives probably the best insight into the subject's genius. There is a complete identification of the author with Mesmer, and one can always see how Mesmer tried various methods to learn in what way his patients could be benefited best. One also sees a keen, intelligent, scientific mind, with humility and criticism, so that one gets an altogether different picture of Mesmer from the usual idea of a mixture of a great personality and a charlatan. The biography of Eddy is interesting in the sense that the author stresses how her work did not really begin until she was quite aged and how her power grew in spite of constant physical infirmities. The account of Freud is perhaps the weakest of all. One gets the impression that the author knew him personally; the biography is a neighborly account rather than a penetrating analysis of a genius.

The book is worth reading.

Diagnostik mit freiem Auge. Ektoskopie und Ektographie mit einem Anhang neuere Tastbefunde. By Eduard Weisz. Fourth edition. Price, 9.50 marks. Pp. 176, with 84 illustrations. Berlin: Urban & Schwarzenberg, 1933.

This is the fourth edition of the author's treatise on what he suggests calling ectoscopy. Ectoscopy is the study of certain phenomena which can be seen by

simple inspection of the surface of the human trunk. To give a typical example, the movements of the intercostal areas during speech may be diagnostically important. By careful and systematized observation, the author has found a number of diagnostically useful signs relative to the visceral organs. Since certain of these phenomena are influenced by paralyses or contractures, the author's methods have a certain, though limited, bearing on neurology.

Weisz presents his material in great detail. His methods are evidently useful since they counteract the modern tendency to neglect observation of the living person in favor of highly technical laboratory methods; but the material which is presented is a little meager for the academic circumstantiality with which it is set forth.

Intracranial Tumors Roentgenologically Considered. By Loyal Davis, M.D., Ph.D. Edited by James T. Case. Price, $10. Pp. 225. Annals of Roentgenology, Volume 14. New York: Paul B. Hoeber, Inc. 1933.

This volume is the fourteenth of a series of monographic atlases issued under the auspices of the *Annals of Roentgenology* and edited by James T. Case, ex-president of the American Roentgen Ray Society. It should be of great interest to all neurosurgeons and neurologists, for the subject is intracranial tumors. The author has done his work well. The illustrations, on which the whole merit of the book depends, are excellent, and the explanatory paragraphs are everything that can be desired, for with each case there is a short but adequate summary of symptoms pertinent to the subject under discussion. Altogether, the book is well worth while.

Recent Advances in Psychiatry. By Henry Devine. Second edition. Price, $4. Pp. 360. Philadelphia: P. Blakiston's Son & Co., 1933.

The second edition of this book differs to some extent from the first. It is not much larger, but considerable new material has been added. Three new chapters have been introduced, dealing with "Germinal Inheritance in the Psychoses" (chapter 2), "Mental Disturbances in Pernicious Anemia" (chapter 11) and "Mental Disorders and Deficient Oxidation" (chapter 17). Much of the material in some of the other chapters has been modified, and the book has been brought up to date. It is a scholarly presentation and one much needed, and it is to be hoped that the author will continue to add new editions from time to time.

The Surgery of the Sympathetic Nervous System. By G. E. Gask and J. P. Ross. Cloth. Price, $4. Pp. 175, with 43 illustrations. Baltimore: William Wood & Company, 1934.

This book contains an acceptable and cautious presentation of the physiology of the sympathetic system and the indications for and results of operations on it. The section on anatomy and physiology is brief and embodies no original observations. Methods of selection of cases for operation are well described, and the authors' operative results are given. The number of cases on which the report is based is somewhat meager, as is the bibliography. A new operative technic for removal of the first and second thoracic ganglia from in front is described. The description of the standard operations is rather brief. The literary style is unusually clear and pleasant to read.

A Performance Ability Scale. By E. L. Cornell and W. W. Coxe. Price, 90 cents. Pp. 88. Yonkers on Hudson: World Book Company, 1934.

This book is both an examination manual, with directions for giving this new series of "performance" tests of intelligence, and a report of their construction or source and their standardization. Like almost all other groups of performance tests, this one is intended primarily for children. Only one of the tests, a picture arrangement, has been especially devised by the authors; the others are taken over from earlier scales.